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June 2-5, 1955

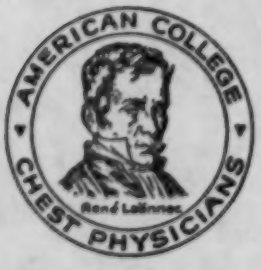
VOLUME XXVII NUMBER 5

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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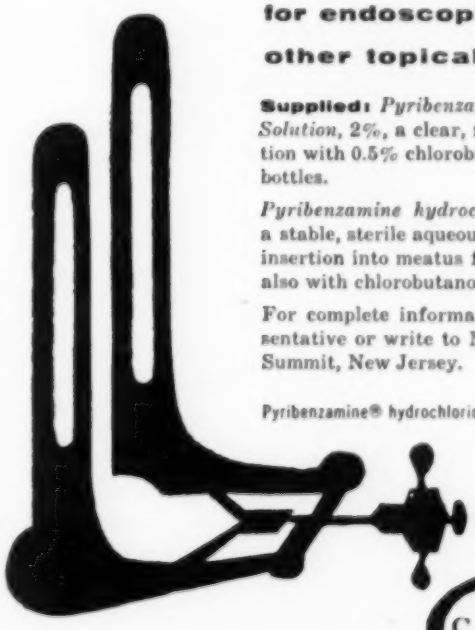

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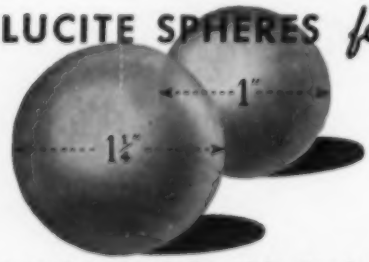

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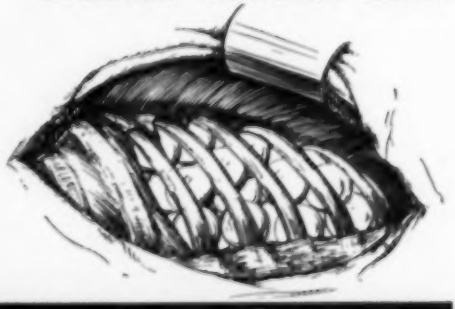

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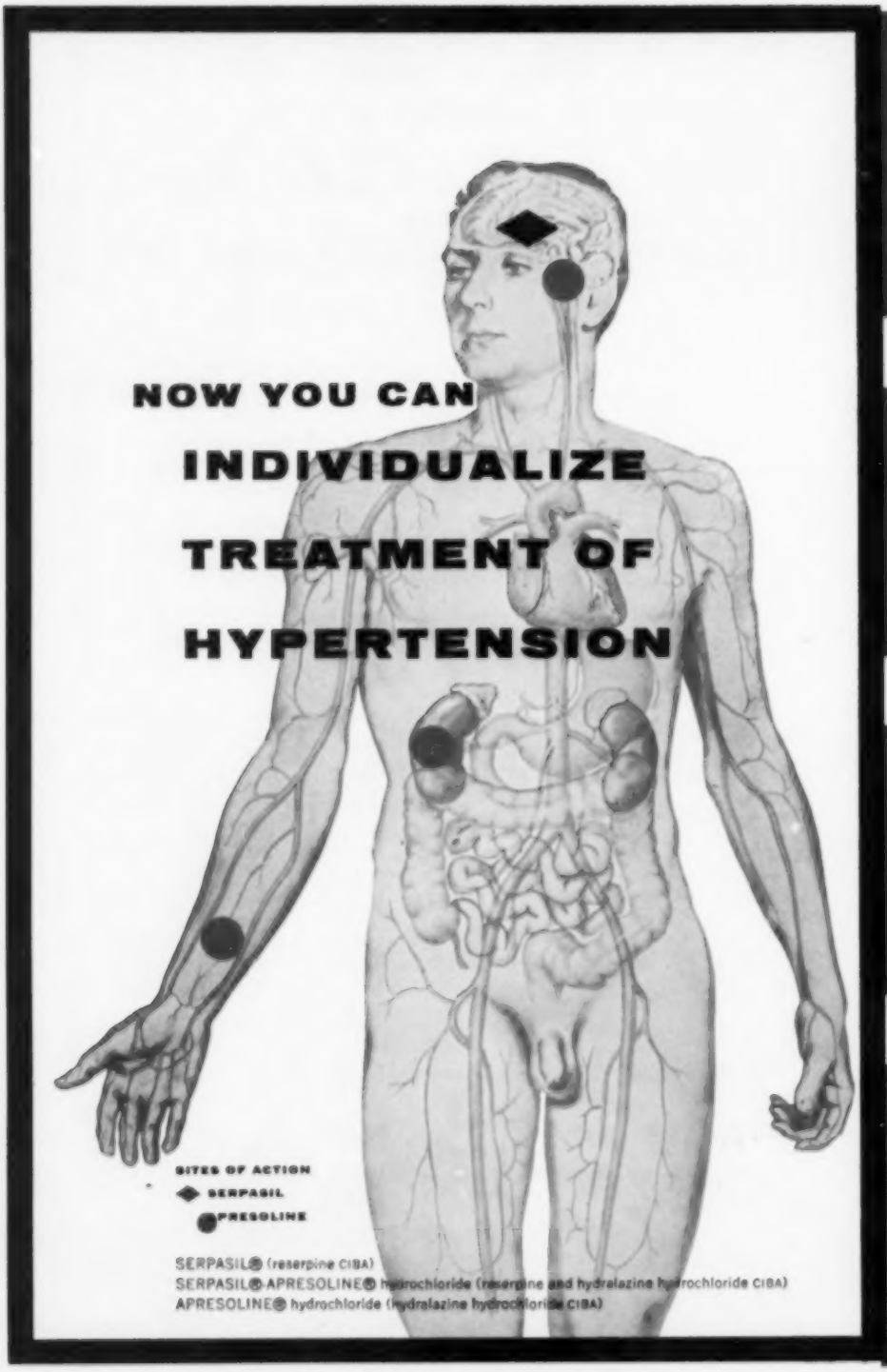
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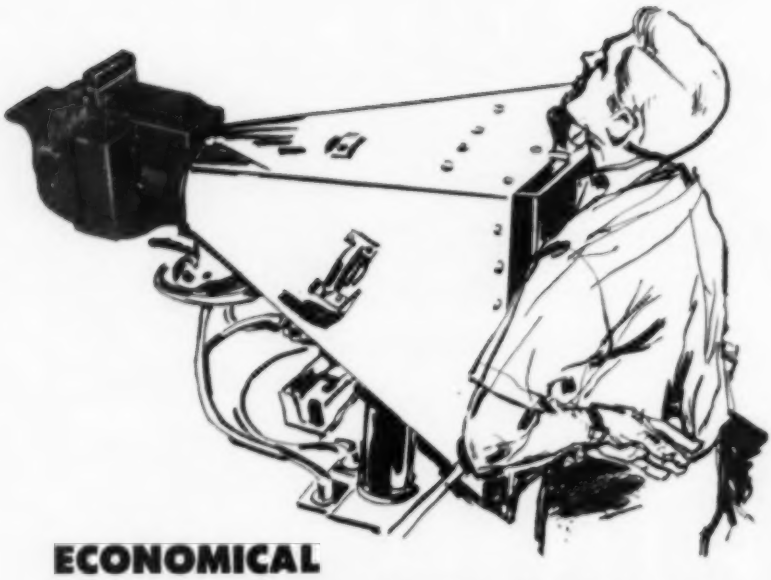

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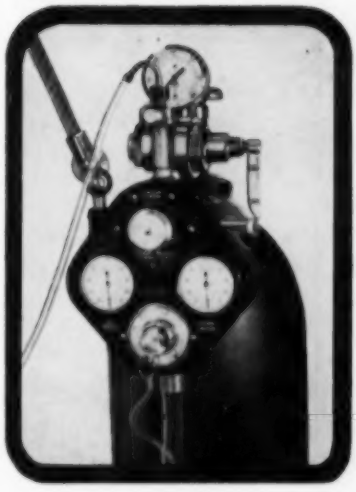

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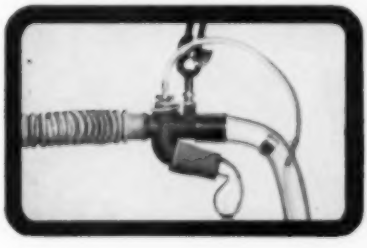

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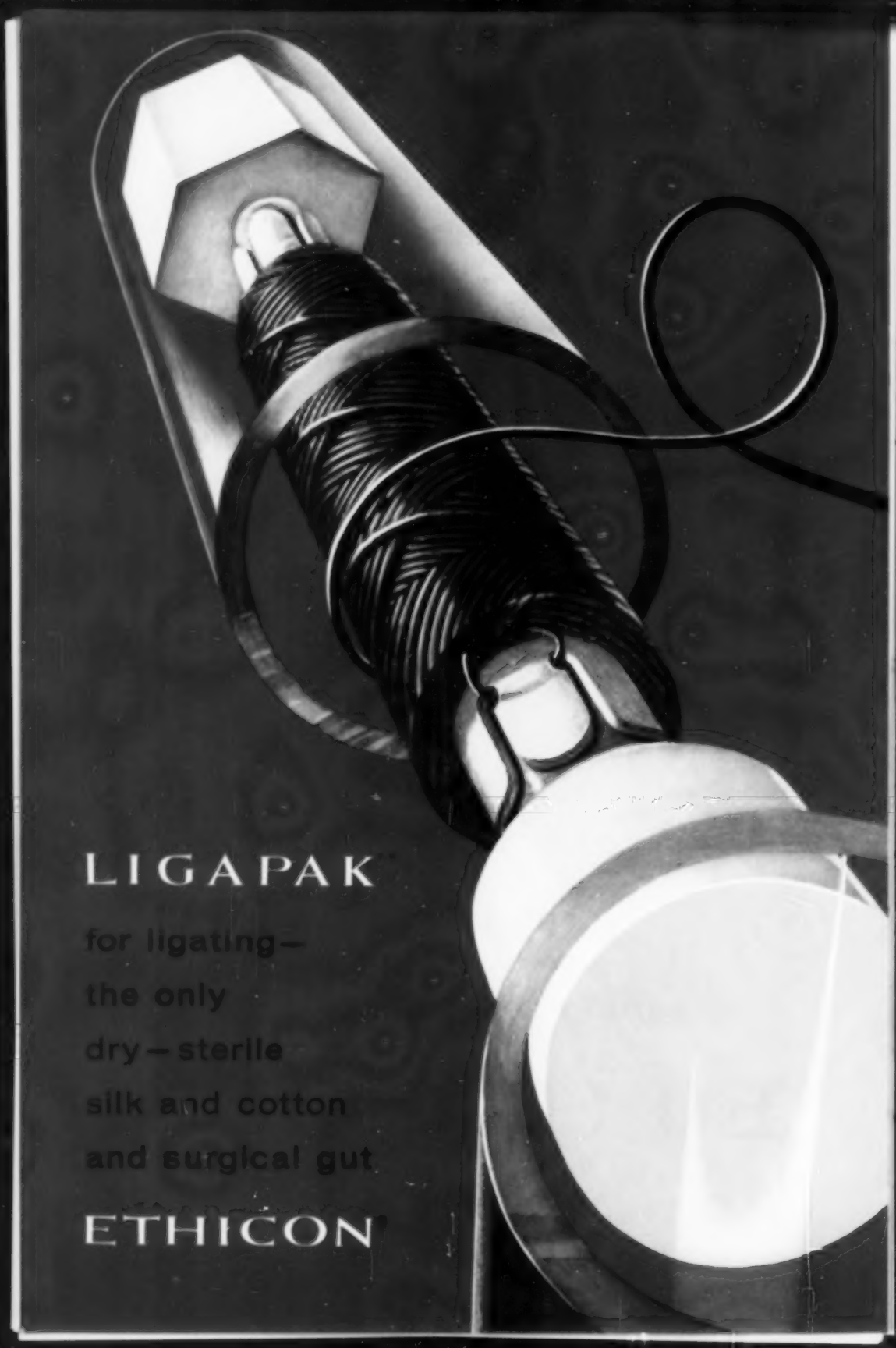
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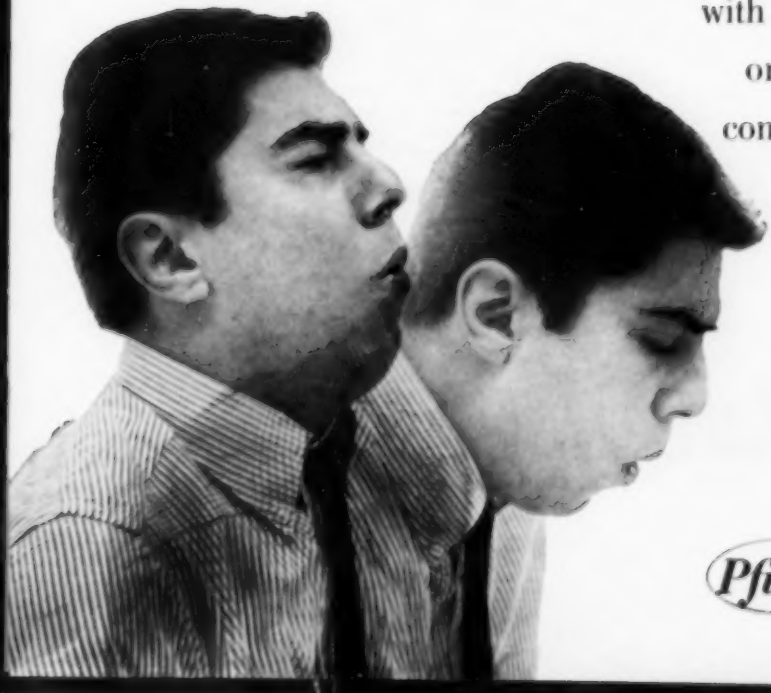

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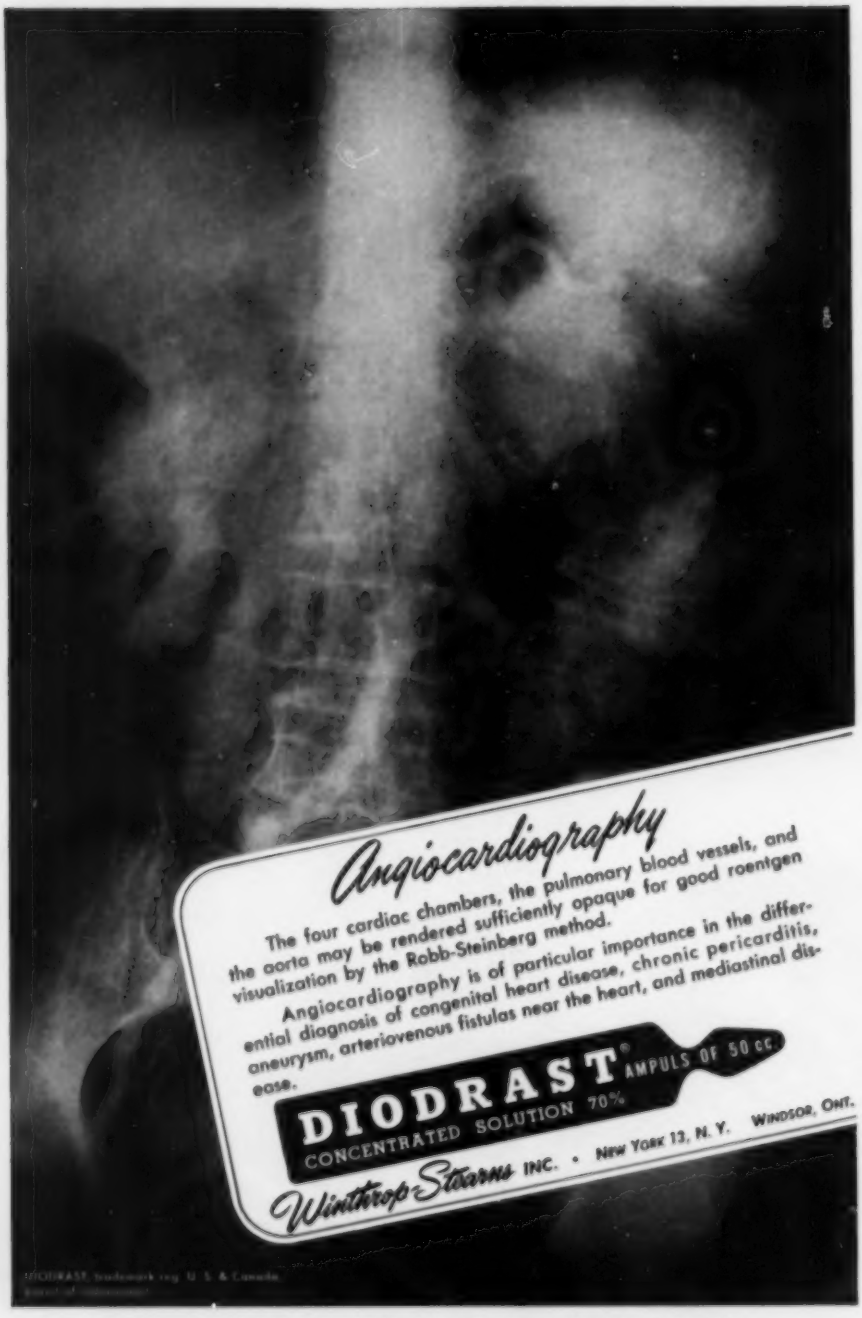
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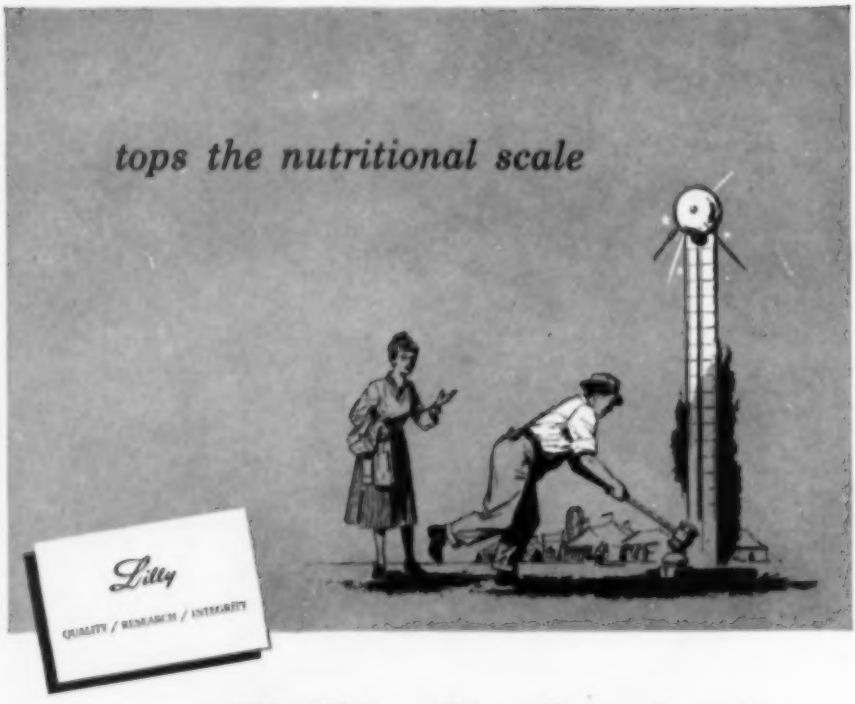

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DISEASES of the CHEST

VOLUME XXVII MAY, 1955 NUMBER 5

The Surgical Treatment of Coronary Insufficiency

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and
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Coronary insufficiency may be defined as an unfavorable balance between the actual amount of coronary blood flow and that quantity required for adequate nutrition of the myocardium. This disparity between supply and demand is reflected clinically in a picture varying from the asymptomatic to the agonizing pattern of angina pectoris. From the viewpoint of pathology, the effects of the inadequate coronary circulation in some cases may cause no discernible damage, in others a discrete necrosis of the subendocardial tissue, or in still others a massive transmural myocardial infarction.

Actually, therefore, the term coronary insufficiency deserves further descriptive expression which qualifies its degree. To this end, Master et al[1, 2] have employed the term "acute coronary insufficiency," designating a transient and partial decrease in blood flow in a segment of a coronary vessel and differentiating this condition from the prolonged coronary arterial insufficiency which results in massive infarction. Even the use of such qualifying adjectives as "acute," "chronic," "transient," and "prolonged" has failed to counteract the basic confusion which follows the application of the generic term "coronary insufficiency" to a clinicopathologic state of such varying proportions. The confusion is compounded when the additional terms of "thrombosis" and "occlusion" are used to imply an ability clinically to recognize the exact precipitating cause of decreased coronary blood flow when such diagnostic acumen does not exist.

For the purposes of this discussion, the term "coronary insufficiency" shall be considered to refer to a chronic imbalance between coronary blood flow and the nutritional demands of the myocardium usually manifested by a previous or by repeated myocardial infarctions, and by continuing symptomatic disability.

Approximately two-thirds of all heart disease is the result of actual or

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relative failure of the coronary circulatory system. In 1949, in the United States, heart disease was responsible for 518,568 deaths, of which 313,757 (60.4 per cent) were attributed to arteriosclerotic heart disease.[3] The next most frequent cause of death was cancer, responsible for 206,325. Master[4] estimates that approximately 800,000 new cases of myocardial infarction appear annually in the United States.

In the vast majority of instances, impaired coronary blood flow results from varying degrees of sclerotic occlusion of the coronary vessels. The causes and speed of progress of this disease are determined by metabolic and perhaps endocrine issues which, for the present, remain obscure. The logical and ultimate solution to the problem of vascular sclerosis must rest with those measures which inhibit its development, and yet in that critical field all prophylactic efforts have been most disappointing. This fact, and the recent dynamic increase in the morbidity and mortality of the disease, particularly when it is referred to the coronary circulation, have been the constant stimulus for newer efforts in treatment.

An understanding of the cardiac pathology and abnormal physiology consequent to the development of sclerosis of the coronary arteries is essential before the role of surgery as a therapeutic tool can be considered fully. Coronary arterial sclerosis most commonly is the result of an atheromatous subintimal degeneration of one or more of the major coronary vessels. Although it occurs in all age groups, it is more frequent in the latter half of life. The actual obstruction to coronary blood flow may arise from the intrinsic atherosclerotic process which eccentrically or annularly elevates the endothelium, or from an associated superficial luminal thrombosis or an intramural hemorrhage. The obstructing lesions almost invariably are limited to the epicardial (visible) coronary vessels and generally occur within 3 to 4 cm. of the coronary ostia. Macroscopically, the involved arteries may not reveal their seriously deranged internal structure. However, they may be greatly thickened and hard. The microscopic changes are limited chiefly to the subintimal and intimal layers where any combination of necrosis, hemorrhage, ulceration, calcification, or connective tissue proliferation may be seen. Medial sclerosis also may involve these vessels and reduce or obliterate their lumina.

Established concepts have related coronary blood flow to the anatomic distribution and the caliber of the vessels, the size of the vascular bed, the head pressure in the arterial system, the vascular resistance, and the venous back pressure. All of these factors are exquisitely interrelated but which one exerts the predominant influence under various normal and abnormal conditions is unknown. It is apparent immediately that the effective caliber of the vessels and the size of the vascular bed are adversely altered by coronary artery atherosclerosis with a consequent reduction in blood flow. However, presumably, there is no fixed relation between this reduction and the degree to which the caliber of the vessel has been reduced. Other factors related to the arterial and venous pressures and vascular resistance are brought to bear which affect considerably the relation of vessel size to blood flow.

The ultimate result of atheromatous narrowing of a coronary arterial segment is modified primarily by the anatomic distribution of the major vessels. Unrolled, fixed, and injected human hearts reveal three basic patterns.[5, 6] In individuals with a predominant right coronary artery, this vessel supplies the right ventricle, the posterior wall of the left ventricle, and the posterior portion of the interventricular septum. In those in whom the left coronary artery is predominant, the left ventricle, the entire interventricular septum, and the posterior portion of the right ventricle are supplied by that vessel. With the balanced type of coronary circulation, each ventricle is supplied by its respective artery. Since atheromatous changes are most common in the left coronary artery, it appears that the potential gravity of coronary artery disease is predetermined at birth and is increased significantly in the 20 per cent of the population who are thought to have a predominant left coronary circulation (Fig. 1).

The end result of coronary arterial sclerosis is further modified by the normally existing but minute intercoronary arterial vessels which function as a collateral system. Although ranging in size from below 40 up to 180 micra, they are capable of considerable dilatation.[7, 8, 9] Actually, these intercoronary vascular communications make up an anastomotic network of considerable size and when artificially or naturally overdeveloped, increase the physiologic size of the vascular bed of the myocardium. While it has been presumed by some that they do not increase the total blood flow quantitatively, they certainly provide a means for the more efficient distribution of blood to areas that otherwise would have been denied adequate nutrition. The circulation provided through these collateral vessels may prevent necrosis of the myocardium when the primary source of blood flow has been gradually and chronically reduced. Even when this is not possible initially because of the acuity or extent of the occlusive process, the collateral circulation may increase locally and reduce the size of the anoxic area. This partial response, however, may fail fully to equalize blood supply and demand, and then the area remains ischemic, a potential focus for the initiation of a fatal ventricular fibrillation.[10] When large portions of the coronary arterial system are involved by the obstructing progress and the collateral system is generally inadequate to supply all myocardial areas, extensive fibrosis results with ultimate disabling or lethal effect upon cardiac output which is expressed usually as left ventricular failure.

However, it constantly must be realized that there normally exist at least two natural mechanisms of myocardial nutrition other than the coronary arterial system. The first, and more important, is the extensive system of vascular communications between the lumina of the various cardiac chambers and the myocardial capillary bed. This represents a vestigial remnant of the original nutritive system and the spongy structure of the primitive heart such as may be seen in the fishes and in certain of the amphibia. The myocardium in these species receives the major portion of its nourishment directly from the blood which it propels and in which it is bathed. Coronary arteries may be rudimentary or absent.

A similar condition is seen in the heart of the 5 weeks old human embryo.[11] This mechanism, in part, persists in the adult mammalian heart, but comparatively is of much less importance. However, in some instances it may be capable of maintaining life and activity (even in man) in the presence of complete chronic obliteration of both coronary arteries.[12]

Figure 2 clearly shows the loose and apparently disorderly arrangement of the intramyocardial vascular channels of the human heart. This is exactly the sort of set-up which logically might have been expected in consequence of its phylogenetic origin. The lack of clear-cut anatomical differentiation between these various vascular elements suggests that naturally or deliberately stimulated alterations in the size of certain of these purely artifically differentially designated vascular channels surely must extend into and involve the others. Thus, we may presume confidently that a demonstrated over-all augmentation of the intercoronary arterial collateral vessels will be attended by a similar overdevelopment of the other blood pathways including those which communicate directly with the cardiac lumina. This phenomenon undoubtedly enhances the potential myocardial nutrition which may be derived from this source in a major degree.

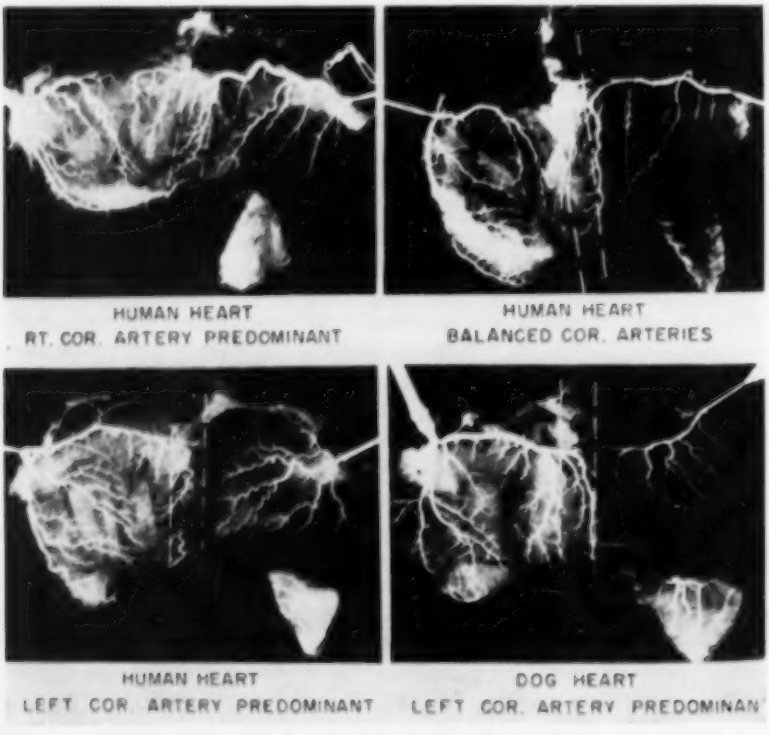


FIGURE 1: Demonstration of the varying types of coronary arterial distribution. (Schlesinger, Gregg's Coronary Circulation In Health And Disease, courtesy of Lea & Febiger).

The second natural source of auxiliary nourishment of the heart is the arteriolar and capillary vascularity existing in the junctional tissue at the base of the heart (junction of the visceral and parietal pericardial reflections). These vessels originate from various intercostal, bronchial, esophageal, and other mediastinal arterial branches. When, due to disease (or surgical trauma), adhesions develop between the visceral and parietal layers of the pericardium, a new capillary vascularity from this source may also become applied to the surface of the heart. This may be considered as forming part of an augmented mediastinal vascular bed. In the presence of a general dilatation of the minute intramyocardial vessels (intercoronary communications), anastomotic communion between the mediastinal and the general myocardial capillary bed becomes free. This concept has been presented previously.[13]

Therapeutic Objectives

The major and logical objective in the treatment of chronic occlusive vascular disease of the heart is correction of the imbalance between the existing blood flow and the nutritional needs of the myocardium. The most obvious method of accomplishing this purpose would seem to involve augmenting the quantity of blood delivered per unit of time by the coronary circulation and improving its distribution throughout the myocardium. Alternatively, blood might be admitted to the myocardial vascular bed by another route. Less desirable would be a method of reducing the nutritional demands of the myocardium so that the limited existing supply might become more nearly adequate for its needs. Either approach to the problem, effectively carried out, should result in the disappearance or significant modification of the manifestations of the disease. When the major objective is beyond realization, modification of the clinical manifestations of the disease without alteration of the basic pathophysiology may become a reasonable and acceptable goal of therapy.

The surgical procedures devised and practiced for the relief of coronary insufficiency may be classified according to the objectives they seek to accomplish. Measures are available which are capable of modifying (1) the manifestations of the disease only, and (2) the actual degree of coronary insufficiency. The latter techniques are divided further into those which diminish the demands of the myocardium, and those which increase the physiologic flow through the coronary vascular bed.

1. *Measures Which Modify the Manifestations of Coronary Insufficiency*

The painful impulses which arise from a chronic imbalance between coronary blood flow and myocardial demand may be blocked by destruction of the sympathetic pathways which mediate pain from the heart. This may be accomplished by postganglionic resection of the upper dorsal and lower cervical sympathetic chain, by division of the preganglionic fibers to these same areas, or by paravertebral injections of alcohol. Obviously, these measures have a limited but sometimes worthwhile applicability in this disease.

FIGURE 2A

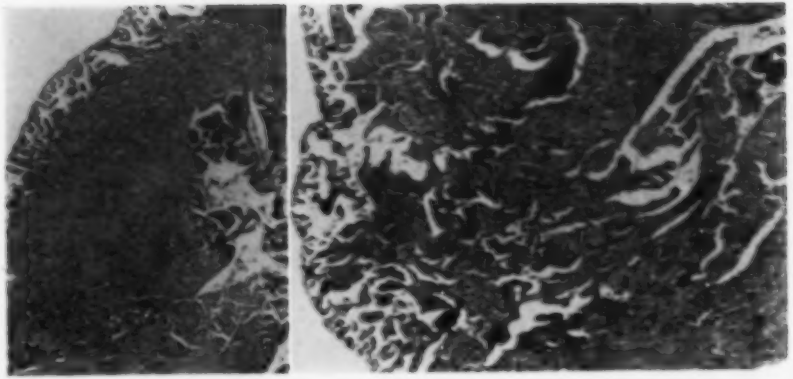
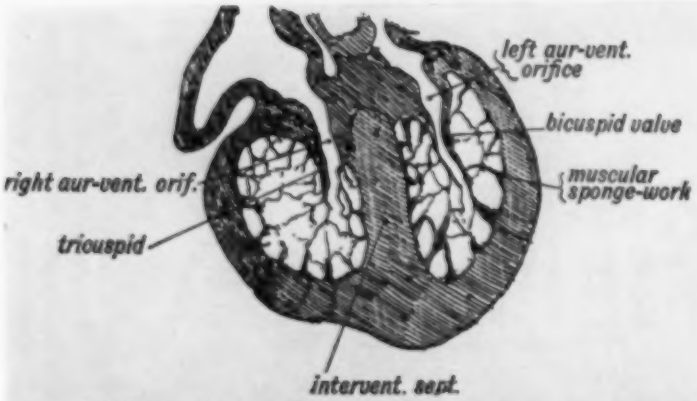


FIGURE 2B



—Section of the Ventricles of the Foetal Heart, showing the Muscular Sponge-work within their Cavities. (After His.)

FIGURE 2C

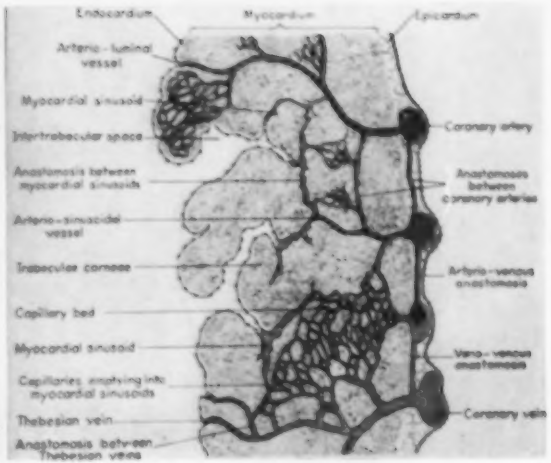


FIGURE 2D

2. *Measures Which Modify the Degree of Coronary Insufficiency*

(a) *By Diminishing Myocardial Demand.* Reduction of cardiac work and hence diminution in the nutritional demands of the myocardium have been accomplished by reducing the basal metabolism by total thyroidectomy, by ligation of the arteries to the thyroid gland, and by destruction of thyroid function by roentgen therapy or the administration of radioactive isotopes of iodine.

(b) *By Increasing the Effective Flow Through the Myocardial Capillary Bed.* This may be accomplished by bringing a new source of vascularity to the myocardium, and/or by stimulating an overdevelopment of the intercoronary collateral circulation.

The intrinsic vascularity of the heart may be increased either at a superficial level or throughout all the layers of the myocardium. Attempts have been made to apply a new source of blood supply to the epicardium by omentopexy, myopexy, pneumopexy, the superficial application of an open excluded loop of vascularized jejunum denuded of its mucosa, and the intrapericardial insufflation of irritants. A variation of these procedures designed to vascularize the myocardium beneath the epicardium has been suggested by Vineberg[14, 15, 16, 17] who has recommended the implantation of a bleeding internal mammary artery into a tunnel created within the thickness of the left ventricular wall. An increased vascularity of the deeper myocardial layers following this procedure is thought to arise from proliferation of small collateral branches of the artery or from a terminal luminal opening.

Beck[18, 19, 20, 21] has developed a method of utilizing the coronary sinus and its tributary venous channels as an auxiliary system for the distribution of arterial blood throughout the full thickness of the myocardium by establishing retrograde flow from the ascending aorta by way of a vascular graft to the coronary sinus. At a second operative stage, the sinus is incompletely ligated at its ostium. This procedure has been modified by Kralik[22] who advises a direct lateral anastomosis between the thoracic aorta and the coronary sinus. At the suggestion of Cowley,[23] we have been successful both in the laboratory and clinically in overcoming the need for a second stage with either of these techniques by applying activated cellophane about the terminal end of the coronary sinus so that its progressive sclerosing action gradually obliterates the lumen, thereby assuring the retrograde passage of arterial blood into the venous channels. However, long term studies by Eckstein et al,[24, 25] and by Bakst et al[26, 27, 28, 29] have shown that such retrograde flow is abolished in experimental animals within three months. Ultimately, the venous radicles of

Figure 2A: Sectional view of the structure of the ventricle of a frog (Rana pipiens). —*Figure 2B:* Enlarged segment showing spongy structure of frog ventricle. The coronary arterial system is relatively primitive in this species.—*Figure 2C:* Sectional view of the structure of the ventricle in a 5 weeks old human fetus. (Keith, Human Embryology And Morphology, courtesy of William Wood and Company, after His).—*Figure 2D:* Diagrammatic representation of the loose and apparently disorderly arrangement of the intramyocardial vascular channels in the human heart. (Gould's Pathology Of The Heart, courtesy of Charles C Thomas).

the coronary sinus become obliterated completely. However, in the meantime, a 4 plus overdevelopment of the intercoronary collateral vessels will have been stimulated (Figs. 3A, B, C, D). In our opinion, the prolonged benefits observed following these operations may be attributed largely to this effect.

Ligation of the coronary sinus or of its major tributary (great cardiac

FIG. 3B

FIG. 3C

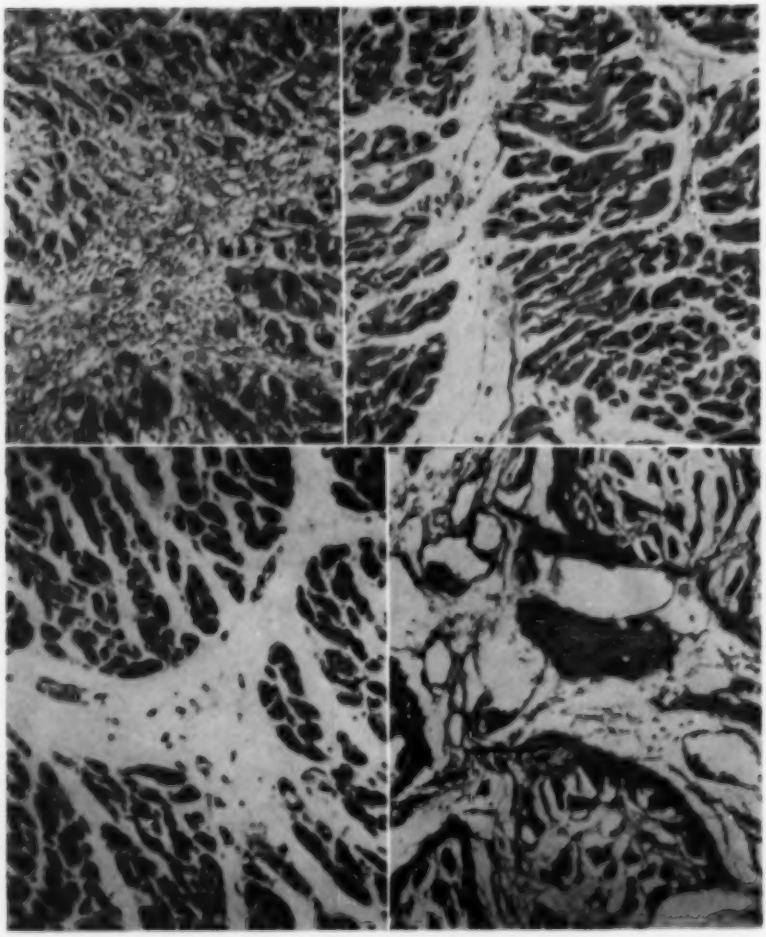


FIG. 3A

FIG. 3D

Figure 3A: 175X magnification of interfascicular space in a 45 year old patient showing normal sized intercoronary arterial channels.—*Figure 3B:* 80X magnification of interfascicular space in a 48 year old patient who had 5 years previously suffered from infarction, and who died 18 days after the first stage of a Beck II procedure. Note great dilatation and increase in the number of the intercoronary channels.—*Figure 3C:* 80X magnification of interfascicular space in a 46 year old patient who died 5 days after the second stage of a Beck II operation. Note great dilatation of intercoronary collaterals.—*Figure 3D:* 80X magnification of interfascicular space in a 54 year old white male who died 3 months after the second stage of a Beck II operation. Note tremendous dilatation of intercoronary vessels amounting to a pseudoangiomatous change. (Bailey's Surgery Of The Heart, courtesy of Lea & Febiger).

vein) has been advised and practiced[30, 31, 32] as a means of altering the venous back pressure and the head pressure in the arterial system in order to stimulate the size and efficiency of the intercoronary collateral system. In our experience (experimentally), this leads to a 2 plus overdevelopment of these vessels.

Discussion

Destruction of the sympathetic innervation of the heart is a palliative measure designed to relieve the pain of coronary insufficiency when it is easily provoked and incompletely benefited by nitroglycerin. Although contrary claims have been made, there is no satisfactory evidence that this method of treatment alters the size of the vascular bed by dilating the arterial or capillary system. The improvement in functional capacity which results in over half of the patients more properly may be attributed to an observed significant decrease in the incidence and severity of bouts of anginal pain. Serious objection has been raised to the modification of this symptom without altering its basic cause since it may serve as a warning against continued and unwarranted activity.

Diminution in thyroid function brings about an over-all decrease in bodily metabolism and, hence, in the demands for myocardial nutrition. Thus, an incompetent coronary circulation may be enabled to meet its minimized physiologic obligations. However, this form of surgical treatment implies the creation of an abnormal metabolic state with disadvantages potentially as disturbing as the disease state it is designed to alleviate. The conversion of vibrant human endeavor to a state of sluggish inactivity is a matter of grave concern, particularly when it cannot be regulated without difficulty and danger. Myxedema, in itself, is a cause of heart disease. Furthermore, presumably hypothyroidism may increase the rate of progress of the established sclerotic processes by its effect upon cholesterol metabolism. Even if this rate is not significantly augmented, the inexorable natural progression of the disease eventually must reduce the coronary blood flow below the level of the reduced myocardial demands. In a strict sense, artificially induced hypothyroidism is but a palliative measure sharply limited in effectiveness by the serious proportion of its side effects. When truly indicated, this form of treatment would seem to be accomplished with less initial risk by the use of radioactive isotopes of iodine than by surgical techniques.

Surgical measures designed to increase the size and rate of the flow through the myocardial vascular bed are best termed *revascularization techniques*. The theoretical potential benefit to be derived from these procedures must be evaluated in lation to the depth and the area of the myocardium receiving the additional blood supply from the new vascular channels, and to the degree to which the natural intercoronary arterial communications become expanded.

The term *surface revascularization* applies to those surgical measures devised to bring an additional arterial blood supply to the epicardium. Included in this group are omentopexy,[33] myopexy,[34] pneumopexy,[35] and jejunopexy,[36] each entailing the grafting of richly vascularized living tis-

sue directly upon the epicardial surface of the ventricle. Arteriolar, or at least capillary, communications develop between the vascular bed of the grafted tissue and that of the most superficial layer of the ischemic ventricle.

The intrapericardial instillation of a powdered silicate produces new arteriolar channels which arise within the inflammatory adhesions which develop between the pericardium and epicardium and, therefore, also is a technique for surface revascularization.[37, 38] Moreover, the work of Schildt, Stanton, and Beck,[39, 40] clearly indicates that powdered asbestos instilled into the pericardium also stimulates at least a 1 plus generalized enlargement of the intercoronary collateral vessels.

Critical questions arise in considering surface revascularization concerning whether the obtained increase in the size of the vascular bed is effective quantitatively, whether it continues to function physiologically after it has been established, and finally, whether it has been applied to vital areas of the myocardium. Although new vascular communications between the graft and the superficial layers of the heart can be demonstrated with dye or radiopaque material, reasonable doubt remains concerning the quantity and direction of blood flow through them. Even the firm proof of a flow of arterial blood through these arteriolar communications would not negate the criticism that perhaps only the superficial layers of the myocardium might be revascularized thereby.

The common observation of isolated subendocardial necrosis occurring in the absence of overt disease of the more superficial layers of the myocardium and of the visible coronary vessels emphasizes the limited protection provided by adequate circulation to the epicardial surface alone. This is not surprising from an anatomic point of view. Fundamentally, the coronary vascular bed is segmental in character since the normal subdivisions of the three main arteries terminate independently in specific layers of spiral musculature and function as end-arteries. A lash of coronary arterial branches is found between each pair of adjacent layers of myocardium, but as groups these are not in free communication with one another. Under such circumstances of anatomic distribution, it is apparent that an increase in the vascularity of certain specific myocardial segments need not increase the vascularity of others.

One, therefore, may question the total amount of benefit so provided unless there is a coincident overdevelopment of the intercoronary collateral system which is capable of distributing some of this new blood to all myocardial layers.

Physiologically, it would appear that the deeper layers of the myocardium are more urgently in need of revascularization than are those close to the epicardium when sclerotic coronary arterial disease is present. Gregg and DePalma[41, 42] have pointed out that the vessels embedded within the deeper myocardial layers are subjected to a higher intramyocardial pressure during systole than are the more superficially placed channels. This implies a greater likelihood of functional impairment to flow and consequently of subendocardial necrosis, particularly when disease of the

vessels is already present.

In spite of theoretical weaknesses in these concepts, attempts to promote extracardiac vascular communications have prolonged life and reduced mortality in the experimental animal when they have been used before or during partial occlusion of a coronary artery.[37, 43] These procedures have reduced the area of induced infarctions, and have enhanced the size of the collateral system. Applied clinically, these same methods have produced encouraging results in decreasing the morbidity and mortality of coronary artery disease.[37, 43] Conceivably, the benefits that have accrued may be based upon the extracardiac vascular communications themselves. However, they may have been accomplished mainly by virtue of an effective augmentation of the size of the intercoronary arterial system and its ability to decrease the threshold of ventricular fibrillation by a more efficient and judicious distribution of blood throughout the myocardium.

Schildt, Stanton, and Beck[39, 40] have indicated that the use of a powdered silicate, asbestos, applied intrapericardially stimulates an expansion of the intercoronary communicating system which was not observed with other substances tested or with other methods of simple surface revascularization. Because only by the existence and function of such a distributing system can blood from a new source be distributed uniformly to the myocardium, and because of the relative ease and safety of the operation, pericardial poudrage probably remains the most satisfactory of the surface revascularization techniques.

The implantation of the bleeding end of the mobilized left internal mammary artery into the thickness of the left ventricular wall has been classified as a surface revascularization technique although the additional blood supply is extended into the deeper myocardial layers. The operation has been advocated by Vineberg on the premise that direct vascular union will take place between the branches and end of the bleeding implanted artery and the smaller tributaries of the coronary arterial system. At the same time, it has been proven satisfactorily by all investigators that this implantation does not produce a purposeless hematoma of the myocardium.

Again the question arises whether this technique results in a quantitatively effective increase in the size of the coronary vascular bed. Actual communications between the systemic artery and the coronary arterial system have been demonstrated by Vineberg in 60 per cent of the experimental animals. However, in our own laboratory[44, 45] grave doubt has arisen as to whether these anastomotic channels are adequate to provide a meaningful increase in blood flow to the myocardium. Flow studies during life indicate that not more than 2 to 4 cc. of blood per minute are distributed through such an implanted vessel to a relatively localized region of the anterior portion of the left ventricle. This implies that while the Vineberg procedure may benefit ischemia which is limited chiefly to that area of the myocardium, it is relatively inadequate in altering the end results of sclerotic disease involving the circumflex branch of the left coronary artery or the right coronary artery. Furthermore, the size of

the lumen of the implanted portion of the internal mammary artery ultimately seems to undergo progressive diminution due to intimal hyperplasia and medial thickening (Fig. 4A, B).

Pratt[46] first demonstrated that rhythmic contractions of the extracorporeal heart of a cat can be sustained by retrograde perfusion of blood into its capillary bed by way of the coronary sinus. Roberts[47] proposed clinical application of this observation, and Beck and his associates[18, 19] developed a satisfactory two-stage technique applicable both in the experimental animal and in man. Basically, the first operative stage consists of establishing an anastomosis between the descending thoracic aorta and a contiguous portion of the coronary sinus by the use of an autogenous vascular graft. At a second stage, when the anastomotic stomata are well healed and the tributaries of the coronary sinus have become adjusted to an increased intraluminal tension, the coronary sinus is ligated incompletely at its terminus. Thus, a retrograde flow system is set up by which arterial blood passes directly from the aorta into the myocardial capillary bed by way of venous radicles.

Kralik[22] has recommended a technical modification in which a direct lateral (side-to-side) anastomosis between the descending aorta and coronary sinus is accomplished without benefit of an intervening vascular graft. This enables one to utilize a smaller arteriovenous fistula since there is less danger of thrombosis of the anastomosis. The small size of the

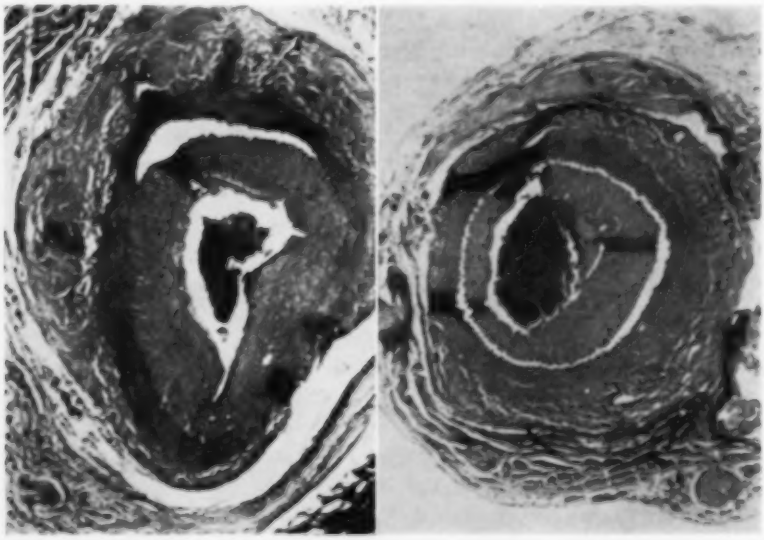


FIGURE 4A FIGURE 4B

Figure 4A: Photomicrograph of first portion of implanted internal mammary artery in a dog after 6 months. Note great reduction in size of residual lumen due to intimal hyperplasia and medial thickening. (Bakst et al, unpublished work).—*Figure 4B:* Similar view of first portion of implanted internal mammary artery in another dog after 6 months. Note great reduction in size of lumen. (Bakst et al, unpublished work).

created stoma avoids the possibility of high output failure sometimes encountered in these cases since a large arteriovenous fistula may persist if the ligature cuts through the sinus permitting recannulation of its lumen.

More recently, in our hands, a further technical modification based upon the gradual sclerosing effect of activated cellophane apparently has eliminated the need for a second stage operation to reduce the size of the terminus of the coronary sinus.

The term *total revascularization* of the heart is applied to the Beck II procedure and its various modifications inasmuch as these measures attempt to make available additional blood supply to its total myocardial mass. The revascularization of the left ventricle, which is the primary objective, extends in part to the right ventricle as well. Initially, arterialization of the coronary sinus establishes a retrograde perfusion of the coronary veins with arterial blood. It has been demonstrated experimentally by Bakst and associates[26, 27, 28, 29] in our laboratory, and by Eckstein and Leighninger,[24, 25] independently, that this arterial blood entering the venous system actually does traverse the capillary bed of the heart. A great reduction in mortality, a decrease in the frequency of ventricular fibrillation, and minimal myocardial infarction have been demonstrated by Beck et al,[20, 48] by Angulo et al,[49] and by Bakst et al,[28] when arterialization of the coronary sinus precedes experimental ligation of a large coronary arterial branch in dogs (Fig. 5A, B, C).

However, it has been demonstrated also that even after ligation of a large coronary arterial branch the retrograde perfusion of arterial blood through the capillary system ceases in the experimental animal after about three months. This is brought about by progressive enlargement of the intercoronary collateral arteries which now bring blood to the area of myocardium which has been deprived of its normal source of blood supply. Later, the smaller tributaries of the coronary sinus system develop medial and intimal hyperplasia and frank thrombosis in response to the persistently elevated pressures (Fig. 6A, B). Ultimately, these changes cause obliteration of the venous vascular channels. From an anatomic standpoint, this development is to be expected since the venous capillary bed, in contrast to the arterial, is not protected by a system of vessels of progressively decreasing caliber but is derived almost directly from large veins and, therefore, bears the full brunt of any significant increase in pressure within these major vessels (Fig. 7A and B). Also, there are intrinsic differences in the structural make-up of arteries and veins which differentially influence their ability to long tolerate arterial pressures.

The ultimate benefit to human patients from total revascularization, therefore, cannot depend upon continued retrograde capillary perfusion. Indeed, it appears to be related more accurately to the overdevelopment of the intercoronary collateral system, and, in part, to the remarkably enhanced extracardiac vascularity which is derived from the pericardial and mediastinal adhesions following surgery. Characteristically, both in the experimental animal and in patients, the produced adhesions can be demonstrated to bear a maze of sizable blood vessels when the anastomosis be-

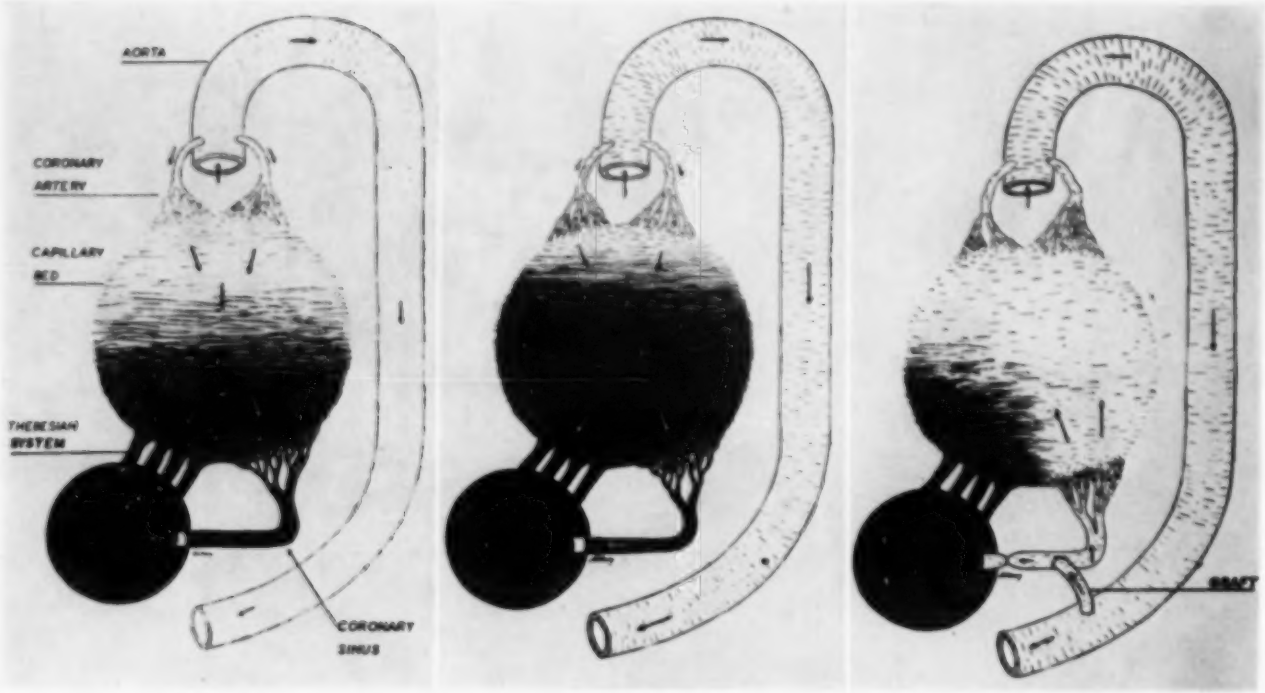


FIGURE 5A FIGURE 5B FIGURE 5C

Figure 5A: Diagrammatic illustration of intrinsic myocardial circulation showing a "balance" between the arterial (light) and the depleted (shaded) blood within the myocardial "marsh" during health.—*Figure 5B:* Illustration depicting excessive proportion of depleted blood within the marsh due to stagnation of blood flow caused by diminution in the effective size of the coronary arterial lumina. The myocardial fibrils must contract essentially under hypoxic conditions.—*Figure 5C:* Increase in the proportion of oxygenated (arterial) blood within the myocardial "marsh" brought about by the creation of a sinus-aortic shunt with later partial ligation of the sinus ostium. The retrograde flow so established has been shown to be transient. (Bailey et al, J. Thoracic Surg., courtesy of C. V. Mosby Co.).

tween the aorta and coronary sinus remains patent, and, in comparison, are strikingly avascular if the graft has become thrombosed soon after its establishment. The functional role of these extracardiac vascularized adhesions appears to be a considerable one since bleeding extensive enough to require replacement transfusions invariably follows their separation in the experimental animal after a successful sinus arterialization. A similar situation has been discovered during reoperation upon two patients for large output failure, respectively fifteen and eighteen months after establishment of the shunt (Fig. 8 and Fig. 9A, B, C, and D).

Ligation of the coronary sinus or a major tributary without arterialization is also classified as a total revascularization technique.[31, 32] Such procedures greatly increase the pressure within the superficial veins of the left ventricle. However, they limit left coronary arterial inflow unpredictably. There is evidence that the chronic passive congestion so created acts as a stimulus to the overdevelopment of the intercoronary arterial system. We consider this overdevelopment to be of 2 plus degree in comparison with the 1 plus augmentation produced by poudrage with a silicate and the 4 plus produced by arterialization of the coronary sinus. The extracardiac adhesions resulting from this surgical procedure are neither as extensive nor as vascular as those following sinus arterialization.

As indicated earlier in this communication and previously,[13] it is felt by the authors that there is no clear-cut anatomical differentiation between the various smaller intramyocardial vascular channels. There are marked ebb-and-flow currents in the course of the circulation of blood through them. It is deemed impossible to augment the size of the collateral intercoronary arterial channels without simultaneously stimulating an enlargement of all the other minute intrinsic myocardial vessels. By continuity

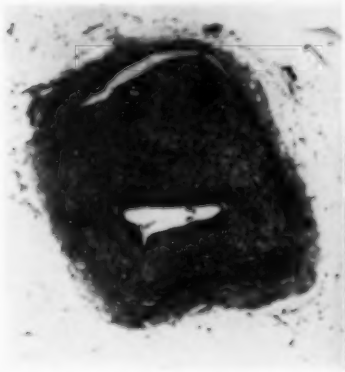


FIGURE 6A

FIGURE 6B

Figure 6A: Extreme reduction in size of lumen of a sizable tributary of the coronary sinus in a dog 6 months following its arterialization. Note great hyperplasia of the intima as well as medial thickening. (Bakst et al, unpublished work).—*Figure 6B:* Section showing the anterior descending coronary artery (central vessel) in a dog, flanked by its two accompanying veins, 6 months after arterialization of the coronary sinus. Note extreme thickening of walls of veins with consequent reduction in the size of the lumina. (Bakst et al, unpublished work).

this process may be presumed to extend both to the luminal communications and to the normal anastomotic mediastinal vessels found at the base of the heart, and also to those found in any newly formed surface adhesions.

Reasoning thus, one must consider that all procedures which have the effect of stimulating or creating intercoronary overdevelopment not only improve the distribution of blood within the various myocardial layers and segments, but simultaneously enhance the effect of the normal or created auxiliary luminal and surface mechanisms of cardiac nutrition (Fig. 8). These secondary circulatory factors independently may be capable of maintaining life indefinitely in extensive progressive occlusive disease of the coronary arteries.[12]

One might consider that the stimulated increase in the effectiveness of these primitive mechanisms of supplying blood to the myocardium had produced a reversion to the "amphibian" type of heart. This raises the question of how useful an amphibian heart would be to a man. Certainly the heart of even the most vigorous amphibian is less competent, especially for the performance of prolonged or violent activity, than is the normal mammalian heart. However, in individuals with coronary arterial disease the existing mammalian heart is markedly deteriorated and its function is unpredictably subject to episodes of painful or fatal depression. In such a person, a more reliable although less efficient heart of amphibian type might well be preferable to the existing diseased mammalian one. This concept is especially applicable in this situation since

FIGURE 7A

FIGURE 7B

Figure 7A: Injection specimen showing structure of the smaller coronary arterial vessels and their relationship to the capillary bed. (Dr. Armand W. Angulo, Hahnemann Medical College, unpublished work).—*Figure 7B:* Injection study of coronary venules showing that the capillaries arise directly from sizable venous branches thus being particularly vulnerable to the effects of intraluminal pressures significantly higher than normal. (Dr. Armand W. Angulo, Hahnemann Medical College, unpublished work).

most of these patients are of middle age or older, and may be willing to accept a life of less than full normal vigor. In any event, there is nothing entailed in any of these revascularization procedures which would seem in any way capable of reducing further the diminished but remaining flow through the natural coronary channels. In other words, any new

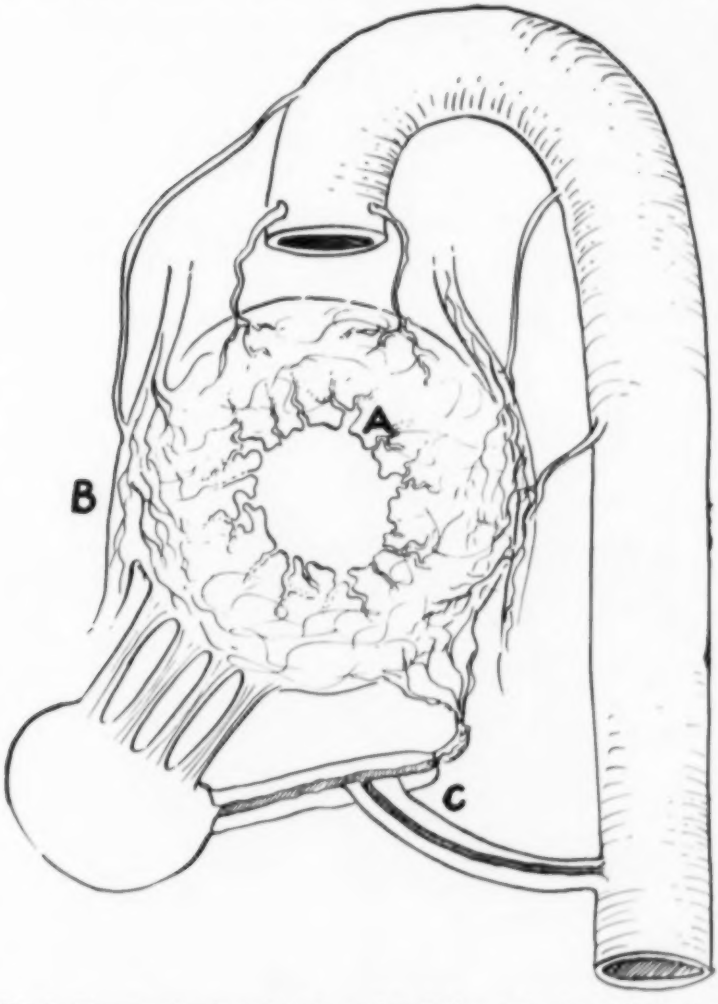


FIGURE 8: Diagram showing what the authors believe to be the ultimate changes in the intrinsic myocardial circulation following arterialization of the coronary sinus. *A*, there is great enhancement in the mechanism of myocardial nutrition from the lumen due to generalized dilatation of the intercoronary arterial channels and all the rest of the intrinsic minute vascularity of the myocardium which connects on one side directly with the various cardiac lumina. *B*, there is an enormous increase in the natural vascularity of all adhesions forming between the surface of the heart and the surrounding tissues. *C*, the coronary sinus tributaries ultimately become obliterated completely. However, the created arteriovenous fistula persists. (Bailey's Surgery Of The Heart, courtesy of Lea & Febiger).

FIGURE 9D

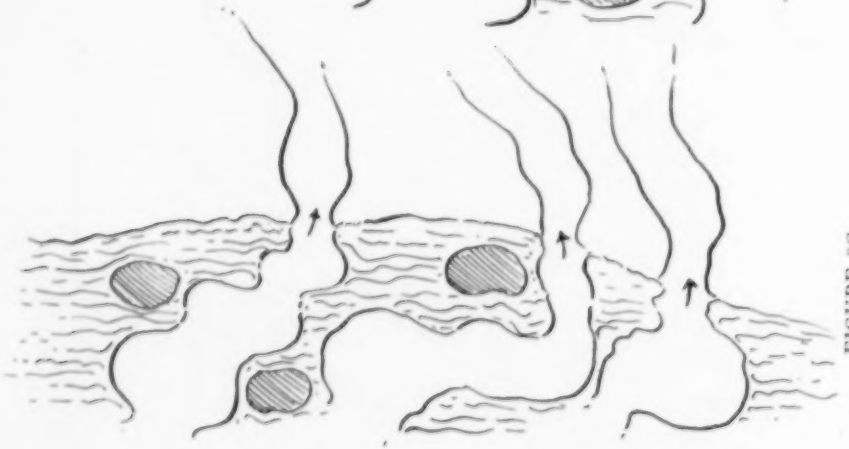


FIGURE 9C

FIGURE 9B

vascularization of the heart, of any type, represents a clear net gain.

The possible mechanisms by which augmentation of the size of the intercoronary arterial channels takes place have been subjected to considerable investigation. Zoll and associates[11, 50] have designated local or generalized anoxia of the myocardium as the chief or primary natural stimulus capable of stimulating overdevelopment of these vessels. Generalized anoxia leading to generalized augmentation of the intercoronary communications may be caused by such systemic processes as anemia, chronic pulmonary disease, or circulatory impairment due to valvular or other type of heart disease. Local elaboration of this system of vessels occurs about areas of marked local ischemia or of frank infarction (usually due to atheromatous blockage of a sizable coronary arterial branch).

However, it is felt that artificial (surgical) stimulation of intercoronary overdevelopment may be related to other factors than pure tissue anoxia. It has been suggested[37, 39, 40, 43] the augmentation in size of these channels observed following the intrapericardial instillation of a powdered silicate may be consequent to the specific chronic irritative effect characteristic of these chemicals. This would seem analogous to the chronic pulmonary

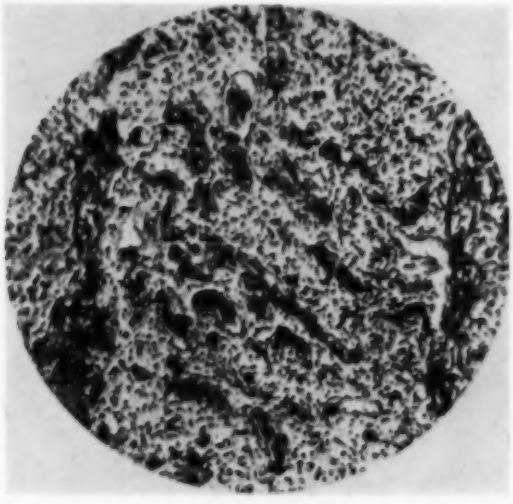


FIGURE 9A

Figure 9A: Great initial vascularity of epicardiopericardial adhesions due to newly formed vascular loops. Subsequently most of these vessels become obliterated. (Forbus, Reaction To Injury, courtesy of Williams and Wilkins Company).—*Figure 9B at left:* Distended capillary bed of myocardial surface following Beck II procedure, and primitive capillary loops forming in surface adhesions.—*Figure 9C:* Direct vascular communion between the congested myocardial capillaries and these primitive loops brings about great enlargement of the latter by distention and prevents their normal involution and disappearance. They then act as "run-off" vessels tending to relieve myocardial congestion.—*Figure 9D:* After the retrograde flow of arterial blood is abolished by progressive obliteration of the coronary sinus venous system, the direction of flow of blood through the markedly vascularized adhesions becomes reversed, blood then flowing from the adjacent tissues into the now ischemic myocardium.

FIG. 10A

FIG. 10AA

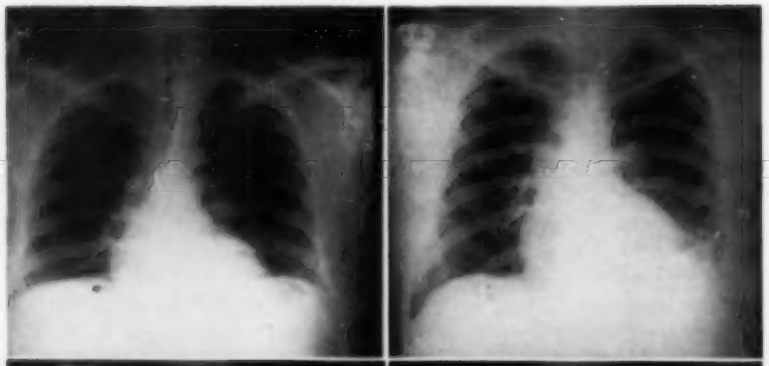


FIG. 10B

FIG. 10BB

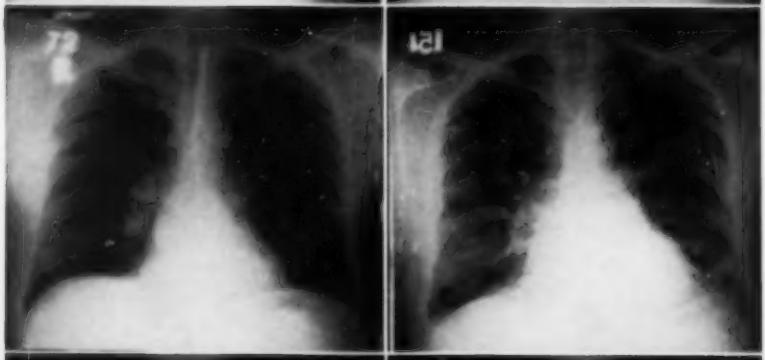


FIG. 10C

FIG. 10CC

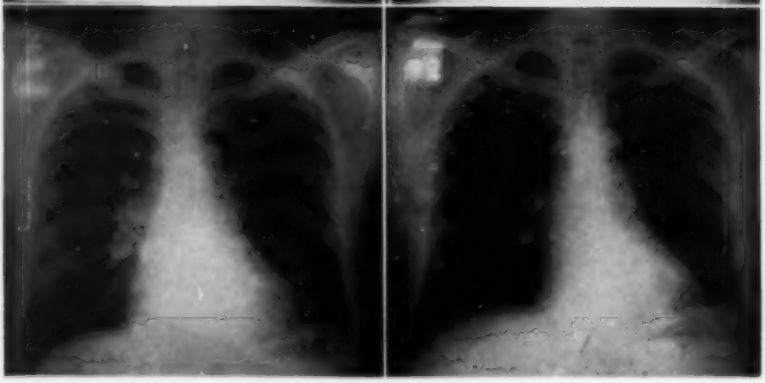


FIGURE 10: Development of progressive cardiac enlargement and large output failure due to creation of a sizable arteriovenous fistula in the Beck II procedure. Correction by ligation of the communicating vascular graft. Serial radiograms in C.T., *A*, taken before arterialization of the sinus and *AA*, 15 months afterward, showing cardiac enlargement due to the excessively large created arteriovenous fistula. Serial radiograms in C.M., *B*, taken respectively before arterialization of the sinus, *BB*, 7 months afterward, *C*, 18 months afterward, and finally *CC*, 3 months after ligation of the communicating graft.

damage caused by inhalation of silicate dusts. There appears to be no primary element of tissue anoxia involved in this process.

On the other hand, simple ligation of the coronary sinus creates a marked degree of myocardial congestion of passive type. Undoubtedly, some actual aggravation of the pre-existing ischemic state may be produced by the pressure of the congested vessels upon the parenchymal myocardial tissue. Frank interstitial edema also may develop. Furthermore, mere prolongation of the time required for drainage of the exhausted myocardial blood due to the partial venous obstruction probably entails some additional tissue anoxia.

However, it would seem reasonable to presume that the long maintained mechanical distention of the capillaries and other small intramyocardial vascular channels might easily bring about a permanent generalized dilatation of these structures. This process logically might become extended to

FIG. 11A

FIG. 11B

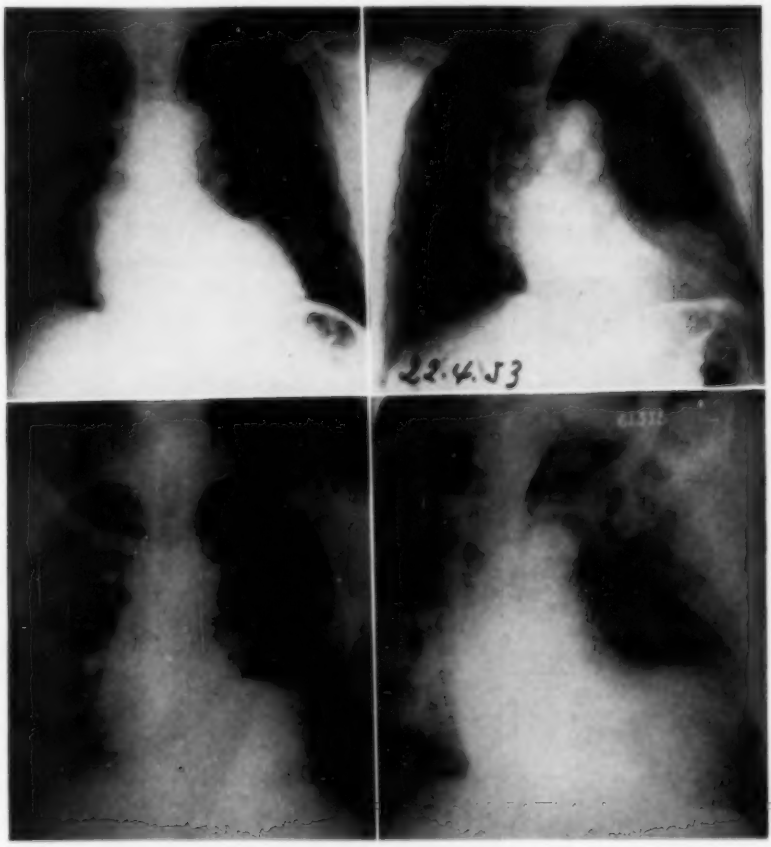
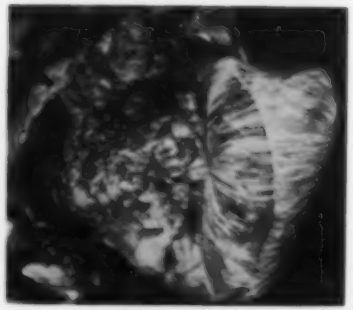


Figure 11A: P-A and right anterior oblique views of heart in V.F. 3 months following myocardial infarction, showing early aneurysm formation.—*Figure 11B:* Similar radiograms taken 10 months later showing increase in size of ventricular aneurysm.

FIGURE 12A



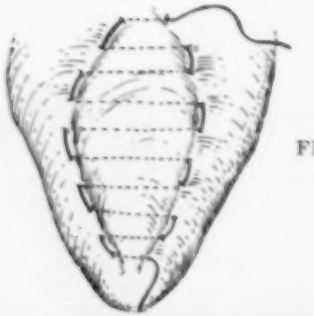


FIGURE 12B

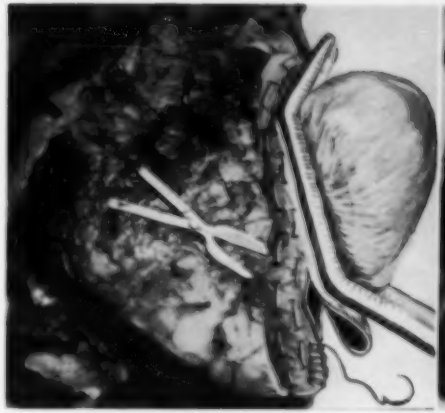


FIGURE 12C

FIGURE 12D

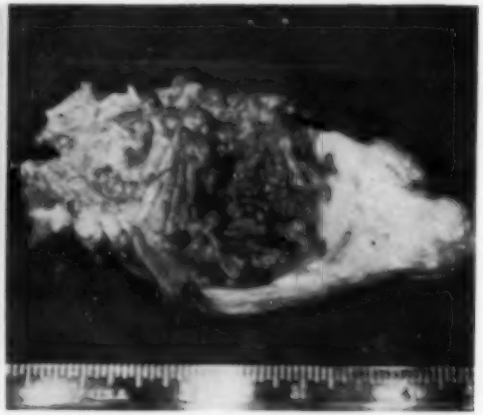


FIGURE 12E

Figure 12A: Artist's reconstruction, upon a photograph of a heart, of the appearance of heart and superimposed ventricular aneurysm as seen at operation in the case of V.F.—*Figure 12B:* Top view sketch showing method of applying first row continuous mattress sutures at the base of the aneurysm. The approximating clamps are not shown. By traction on the ends, the aneurysmal walls become approximated at its base.—*Figure 12C:* Sac being resected distal to two rows of mattress sutures; the outer row was placed in interrupted fashion.—*Figure 12D:* Cut myocardial edges finally oversewn.—*Figure 12E:* Resected specimen of aneurysm alongside an inch ruler. (Bailey's Surgery Of The Heart, courtesy of Lea & Febiger).

involve their cardiac luminal apertures, thus enhancing the size of these communications. Indeed, this was the original concept and objective of Gross and associates[39] who investigated the effects of experimental ligation of the coronary sinus in 1937.

Furthermore, such a generalized turgid congested condition of the myocardial capillaries would seem materially to influence the development of adhesions forming upon the surface of the heart. Normally the initially very numerous proliferated capillary loops characteristic of early adhesion formation undergo prompt involution and ultimate obliteration. Unless there is a stimulus toward persistence, such as may be seen in certain chronic inflammatory or infectious states, such adhesions soon become relatively avascular. However, the existence of distended capillaries upon the surface of the heart would seem to facilitate or predispose toward excessive vascular communication by way of the forming capillary loops with the intrinsic vascularity of the adjacent superimposed or "grafted" extracardiac tissues. A tendency toward persistence of these congested "hypertensive," and undoubtedly relatively large vascular communications then must logically be expected, not only because of the increased size of the anastomotic vessels but also because they would tend to function as a partial "run-off" for the congested myocardium. In time, with progressive overdevelopment of the non-obstructed deeper myocardial venous drainage channels, the passive myocardial congestion must tend to diminish and ultimately disappear. Then, the free vascular communion between the extracardiac "grafted" tissues and the superficial layers of the myocardium might well permit reversal of the previous direction of flow so that arterial (capillary) blood might pass from the graft into the ischemic heart muscle.

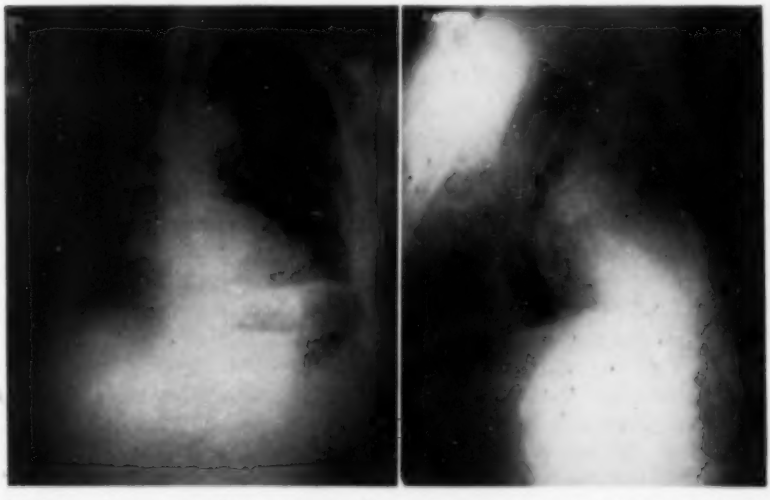


FIGURE 13: P-A and right anterior oblique radiograms of V.F. taken 6 weeks following surgery. Note disappearance of aneurysmal bulge from cardiac outline and over-all reduction in the size of the cardiac silhouette.

A similar explanation may be advanced for the demonstrated great augmentation (4 plus) of the intercoronary vessels following retrograde perfusion of the coronary sinus by a created aortic fistula. However, the resultant myocardial vascular congestion is even more pronounced and persistent (Fig. 5C) due to the constant addition of an appreciable amount of arterial blood to the limited capacity of the myocardial vascular bed (at least 200-500 cc. per minute). Therefore, the physical "dilating" effect upon the size of the intramyocardial vessels due to mechanical congestion must be enhanced correspondingly. Again, once the initial retrograde transvenous perfusion becomes abolished by progressive obliteration of the tributaries of the coronary sinus, all of the enlarged luminal and surface vascular pathways, formerly run-off channels, become available for use as afferent passages or sources by which blood can reach the ischemic myocardium (Fig. 8 and Fig. 9A, B, C, D).

Both the surface and the total revascularization techniques alter the effective anatomic distribution of the coronary vessels and increase the size of the vascular bed. Their effects upon arterial head pressure, vascular resistance, and venous back pressure are either incompletely understood or unrecognized. It is apparent that a thoroughly dependable surgical procedure must influence favorably either all or the most predominant determinants of coronary blood flow. However, it is entirely reasonable that the major initial efforts in the field should be dedicated to the obvious objective of increasing the size of the vascular bed.

Surgical Experience

Because theoretically, and in the experimental laboratory, arterialization of the coronary sinus most profoundly increases the size of the coronary vascular bed, we have applied the technique clinically in a total of 71 patients. Of these, 53 have had the two-stage Beck II procedure which employs a vascular graft placed between the aorta and coronary sinus, and 18 have had the Kralik modifiaction which eliminates the use of the graft.

There have been 8 operative deaths in the 53 patients subjected to the Beck II procedure, 6 prior to the completion of the second stage and 2 subsequent to it. In 8 of the series, the vascular graft was found to be thrombosed at the time of the second operative stage. Two patients developed high output failure within fifteen months because of the excessive size of the arteriovenous fistula so created but improved immediately after the coronary sinus was completely ligated at a third operation (Fig. 10).

There has been one operative death in the 18 patients subjected to the Kralik modification of the Beck II procedure, which creates a smaller arteriovenous fistula that in our experience has neither become thrombosed nor produced high output failure. The ability gradually to obliterate the coronary sinus ostium with activated cellophane, thus reducing the operation to a single stage technique, unquestionably will decrease further the risk and morbidity involved in the Kralik modification. All surviving patients have been clinically benefited with respect to the cardiac condi-

tion, although one developed a spinal cord complication, presumably due to too extensive mobilization of the aorta with development of a paraplegia. This generally satisfactory clinical experience certainly is related to judgment in patient selection and to the choice of the operative technique.

Criteria for Selection of Cases

In our present state of knowledge, it would seem that the surgical treatment of chronic coronary arterial insufficiency should be directed toward those patients whose clinical pattern implies an ominous prognosis, or whose manifestations seriously interfere with their ability to meet the requirements of ordinary living. Although occlusive coronary artery disease always implies an uncertain prognosis and the possibility of sudden death, surgery cannot be advised lightly merely because of the presence of the disease alone. However, it seems reasonable to suggest that the occurrence of a definitely established myocardial infarction is a sufficient manifestation of an ominous failure of the coronary circulation to serve as a primary indication for surgical therapy particularly when it is found in patients who have not yet reached 50 or 55 years of age and hence presumably are suffering with a greater than an average tendency toward progression of the disease.

The more common indication for surgical treatment is easily provoked angina pectoris which seriously limits ordinary activity. Since this clinical picture often is encountered just prior to the development of a myocardial infarction, it is necessary to establish the fact that the incapacitating nature of the angina pectoris has been a chronic event. Under no circumstances should surgery be considered within several months of an episode of acute myocardial infarction. Although the Kralik-Beck technique promises the most extensive revascularization, it remains the most trying procedure to withstand surgically. Hence, it is best limited to patients less than 55 years of age who have not suffered from more than two previous episodes of infarction, who are not handicapped by other severe systemic disease such as diabetes or hypertension, and who do not have more than a 20 per cent enlargement of the heart (radiographic demonstration). Furthermore, since this technique creates a fistula between the aorta and coronary sinus, it should not be applied in patients with past or present evidence of congestive heart failure, or even severe reduction in myocardial reserve.

While a lesser degree of revascularization (1 plus) is promised by the intrapericardial insufflation of a powdered silicate, this entails only a relatively simple surgical technique that can be applied through a limited extrapleural anterior thoracic incision. This is the more justifiable procedure in patients over 60 years of age who have had more than two myocardial infarctions, a greater degree of cardiac enlargement, or a history of previous congestive heart failure.

Undoubtedly there is an intermediate group of patients in whom either the Vineberg technique or the combination of pericardial poudrage and coronary sinus ligation (Beck I procedure) should be used. Where the

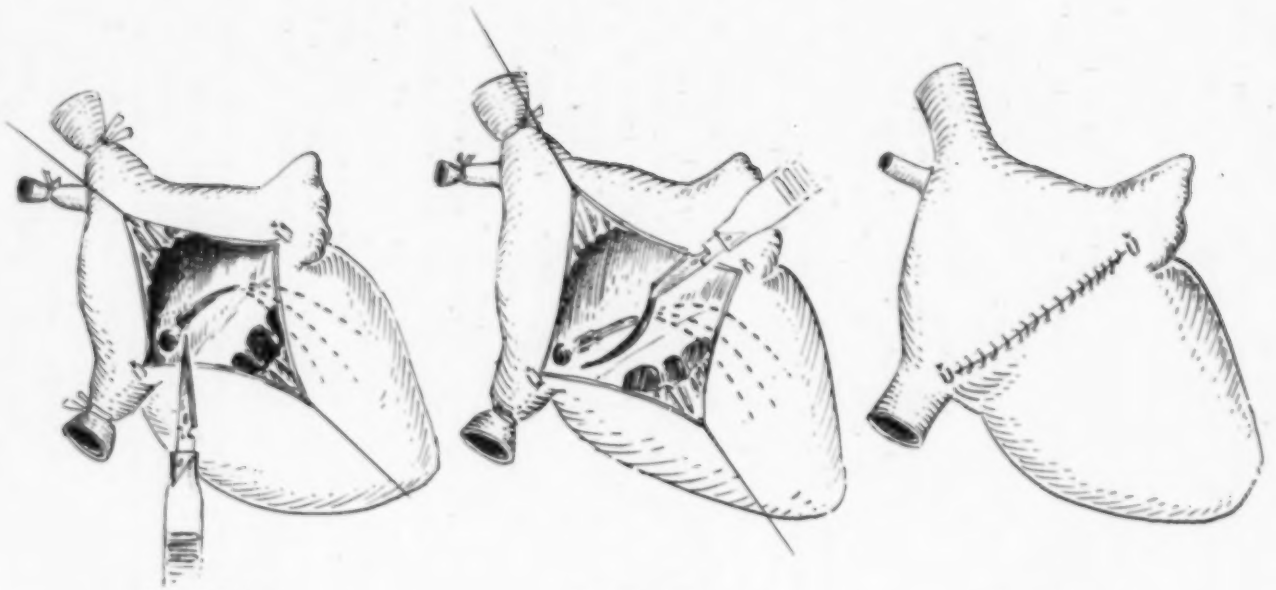


FIGURE 14A FIGURE 14B FIGURE 14C

Figure 14: Experimental creation of complete heart block. *A*, right atrium opened under hypothermia (or more quickly at normal temperatures) after obstructing vena caval flow. Location and course of A-V conduction system indicated. *B*, division of common conduction (A-V) bundle. If septum is penetrated inadvertently, it is repaired immediately by suturing. *C*, atrial wall closed and circulation restored. Many animals die within 24 hours due to onset of acute ventricular fibrillation.

myocardial involvement is highly localized to the anterior surface of the left ventricle and the patient is not considered an adequate risk for total revascularization, the Vineberg operation may be considered. On the other hand, the Beck I technique may be used where the need for total revascularization exists but the past history of, or present, or incipient congestive heart failure contraindicates the creation of an arteriovenous fistula.

Surgical Complications of Coronary Arterial Disease

Ventricular Aneurysm—In view of the unhappy prognosis associated with a ventricular aneurysm complicating coronary arterial disease, it appears that the very presence of the lesion is the indication for its sur-

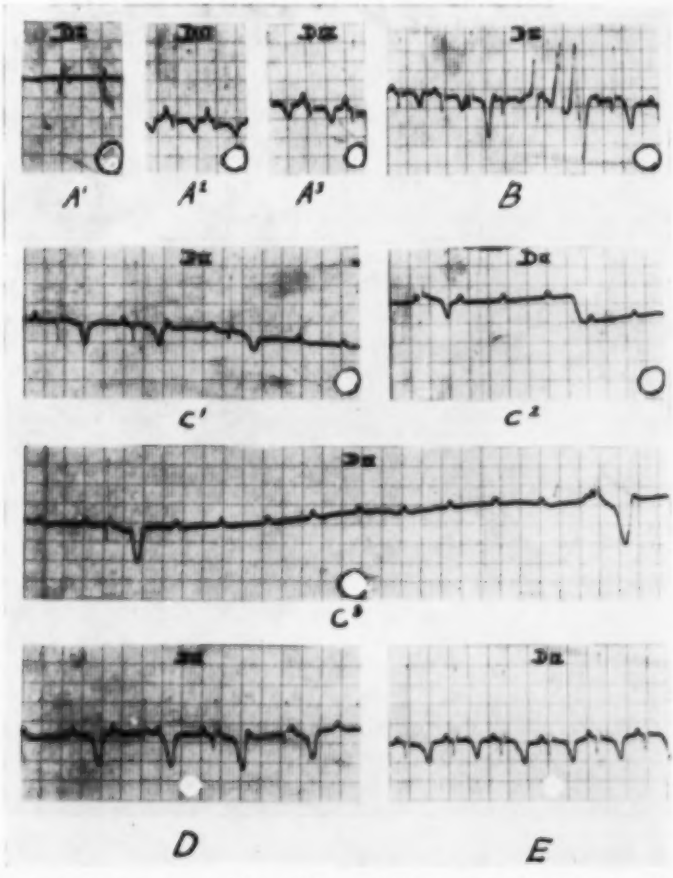


FIGURE 15: Electrocardiographic studies of Aixala and Sanchez showing the creation of complete heart block in a mongrel dog, and its correction through the formation of an artificial bundle of kent. *A*, leads in the normal dog. *B*, extrasystoles with the knife in the left ventricle. *C*, complete heart block created by surgical division of the bundle of His. *D*, during suturing of muscle graft from left auricle to left ventricle. *E*, reconversion to normal sinus rhythm. (Courtesy of Drs. Aixala and Gabriel Sanchez, Havana, Cuba, unpublished material).

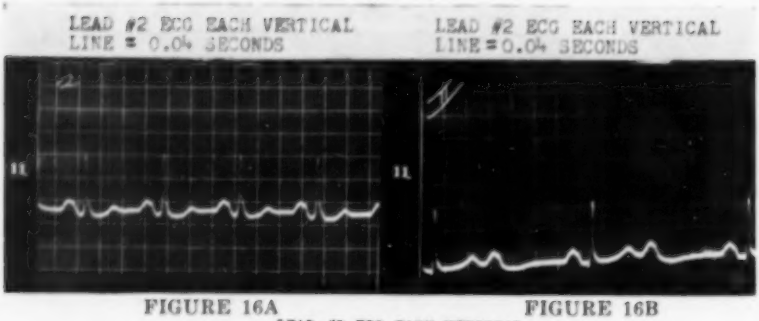


FIGURE 16A FIGURE 16B

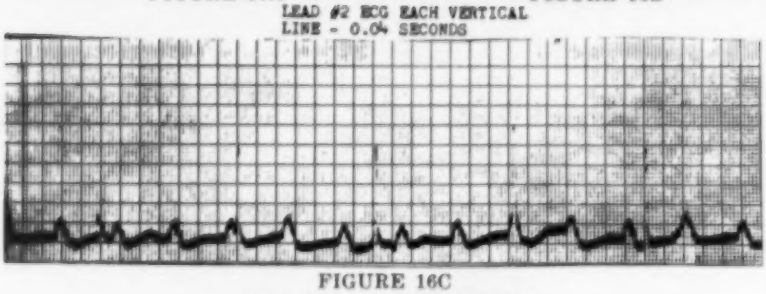


FIGURE 16C

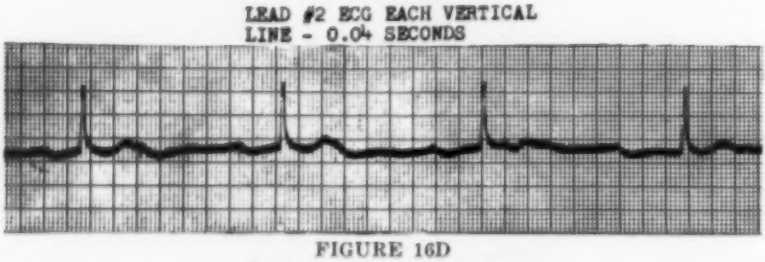


FIGURE 16D

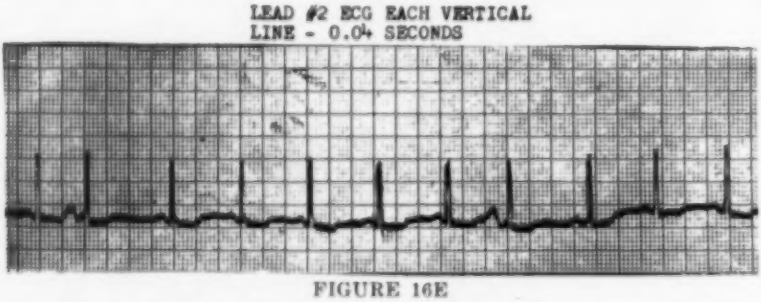


FIGURE 16E

Figure 16: Correction of spontaneously appearing heart block in C.R., a 36 year old rheumatic white male. *A*, lead 2 of electrocardiogram taken 2 years previously. Note normal conduction time with P-R interval of .22 sec. *B*, 2 to 1 heart block seen in C.R. on Nov. 10, 1954. *C*, 4 to 1 heart block seen in C.R. on Nov. 15, 1954. *D*, lead 2 taken 24 hours after surgical creation of bundle of Kent. There is no observable change in conduction mechanism. *E*, electrocardiogram taken 6 days postoperatively shows reestablishment of atrioventricular conduction. Note that P-R interval is .12 sec. in duration. Occasional premature atrial contraction is present. QRS complexes are not bizarre.

gical removal. Although present experience in the successful removal of a ventricular aneurysm is limited to the one patient (apparently the first in medical annals) operated by one of us (C. P. B.) on the 15th of April, 1954, at the Hahnemann Hospital, in Philadelphia,[13, 51] significant knowledge was obtained in the problem of patient selection for such a procedure.

Case Report: V. F., Case No. 54-04387, a 56 year old coffee planter, had suffered a myocardial infarction in January, 1953. Progressively increasing disability from persistent anginal syndrome and the appearance of evidences of congestive heart failure led to consideration of definitive excision of an enlarging anterolateral ventricular aneurysm (Fig. 11A and B). A persistent diastolic gallop rhythm existed prior to operation. At the time of surgery, a large noncrushing clamp was applied across most of its poorly demarcated base. After placement of two rows of mattress sutures, the sac was excised and the cut edges of the myocardial wound were approximated with running sutures (Fig. 12A, B, C, D and E).

Comment

The convalescence was essentially uneventful. Gallop rhythm disappeared within one week. Marked clinical improvement ensued and has persisted. The heart size became reduced markedly (Fig. 13).

Since no revascularization procedure was carried out, it would seem that the observed benefit was brought about entirely by the removal of the deleterious physiological effects produced by the paradoxically pulsating aneurysmal sac. This experience suggests that patients with enlarging aneurysms and those with symptoms of progressive circulatory impairment with a coexisting cardiac aneurysm should have an opportunity to have surgical intervention at an earlier stage.

As a general rule, overt congestive failure and gallop rhythm are recognized as basic contraindications to cardiac surgical procedures. However, in patients with sizable ventricular aneurysms these clinical findings fail to respond to the ordinary measures of therapy and, although deterrents to the successful conclusion of the operation, represent an indication rather than a contraindication to surgical intervention.

Heart Block and Adams-Stokes Syndrome—Since the specialized group of myocardial fibers which make up the so-called bundle of His represent the only normal myocardial connection between the musculature of the atria and the ventricles, impairment of its physiological or anatomical continuity will tend to dissociate their respective functions.

While blockage of transmission of the excitation impulse through the bundle of His and its branches may be brought about in several ways (congenital defect, surgical or accidental trauma to the heart, involvement by a rheumatic nodule), the most frequent cause of such interference is coronary atherosclerosis. Either ischemia or frank infarction involving the septum may affect the conduction system producing various types of bundle branch block, delayed conduction, or even complete heart block. In this latter condition, the ventricles develop an independent contraction rhythm with a rate which may vary from 30 to 50 per minute. Meanwhile, the atria continue to contract at their own usual rate (70 to 100 per minute). In some individuals, the type or degree of block may vary from day-to-day or week-to-week.

FIGURE 17B

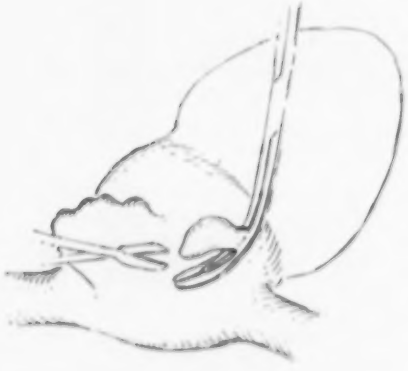


FIGURE 17A

FIGURE 17D

FIGURE 17D

FIGURE 17C

While those persons who have a permanent complete heart block seem to do reasonably well for prolonged periods of time, the over-all life expectancy in cases due to atherosclerotic heart disease is estimated to be between 12 and 24 months. Furthermore, these individuals experience a significant loss of reserve for vigorous activities. Perhaps this is due to an inability to increase their cardiac output on demand by an acceleration of rate. In some patients, transient asystole may occur resulting in fainting and convulsions (Adams-Stokes syndrome).

On the other hand, individuals who exhibit heart block which varies from day-to-day and from week-to-week tend more frequently to develop such episodes of transient asystole, any of which may eventuate fatally from severe depression of ventricular irritability due to the prolonged anoxia, or from the sudden onset of ventricular fibrillation.

Hence, it was deemed desirable to attempt to develop a method of creating surgically a new conduction pathway between the atria and ventricles. Anomalous congenital communications of this type are occasionally seen (bundle of Kent[52]). Such an abnormal conduction pathway usually represents an area in which the development of the atrioventricular fibrous ring (annulus fibrosus) has been deficient so that a direct (embryonic) atrioventricular myocardial communication persists in addition to the normal bundle of His. In such cases, the observed time of atrioventricular conduction (P-R interval in the electrocardiogram) is observed to be abnormally short. Presumably this is to be explained by the passage of the excitation wave from atrial tissue directly into the continuous muscle fibers of the ventricle without need for passage through the node of Tawara (A-V node) and the common conduction bundle. It was deemed possible to create a similar communication surgically.

Experimental Technique

Complete atrioventricular dissociation was brought about in experimental animals (mongrel dogs) by surgically dividing the common conduction bundle as it passes along the lower interatrial septum. This was done with the venae cavae temporarily occluded under direct vision (Fig. 14A, B, C). Using this technique, we have been able to produce a complete and lasting heart block in several dogs, which we have employed in testing various grafting techniques. At a later date we have carried out procedures designed to correct the block.

Prior to the initiation of this investigation (September 1954), and unknown to us, Aixala and Sanchez,[53] in Havana, Cuba, had independently undertaken a similar study (March 1954). We in no way desire to deprive them of proper priority for this concept or for the experimental

Figure 17: Technical steps in the creation of a "Bundle of Kent." *A*, isolation of a portion of the right atrial wall with formation of pedicle. *B*, oversewing of the defect and elevation of a partial thickness of the ventricular wall below the coronary artery. *C*, insertion of the everted atrial pedicle into the ventricular bed. Note the sutures placed around the ventricular flap to guarantee complete surface apposition of the "sandwiched" graft. *D*, second full thickness pedicled graft raised from right atrial wall for implantation without eversion. *E*, closure of second atrial incision and insertion of non-everted "isoperistaltic type" graft into a myocardial tunnel.

demonstration of its validity. Figure 15 clearly shows the restoration of atrioventricular conduction in an 11 lb. mongrel dog in which they had previously produced heart block at the same operation by the instrumental transventricular technique of Sodi Pallares.[54] Our work has been directed toward producing a complete and permanent block at one operation, and then, after a suitable interval has elapsed to avoid any possibility of spontaneous remission, toward producing a permanent correction at a second procedure.

Case Report: On November 15, 1954, at Hahnemann Hospital, in Philadelphia, an operation to form an artificial bundle of Kent[52] was done on C. R., Case No. 54-13211, a 36 year old white male with a heart block which varied from complete to 2 to 1 (Fig. 16A, B, C, D, E). A portion of the right atrial wall was excluded from the circulation by a nonerushing clamp technique. This elongated excluded segment was then separated from its atrial attachment except at one extremity. The residual defect in the atrial wall was closed by sutures.

FIGURE 18: Photograph of operative field in C.R. showing diagonally placed (arrows) strip of mobilized atrial wall.

Then, a selected portion of the thickness of the right ventricular wall was split and the epicardial portion was elevated. After freshening both its epicardial and endocardial surfaces, the end of the pedicled atrial tissue was placed between the two layers of the ventricular wall in "sandwich" fashion. Several interrupted sutures were placed to maintain the displacement of the atrial tissue permanently (Fig. 17A, B, C, and D). A second longer pedicled graft of atrial tissue was prepared and placed similarly but without eversion.

While no change was noted in the patient's cardiac rhythm or conduction for five days following operation, suddenly on the sixth day a nearly normal type of atrioventricular conduction developed with an increase in ventricular rate from 50 to 82 per minute. The QRS complexes presented a fairly normal over-all configuration, but the P-R interval was only .12 second. It had been .22 second in duration on examination two years previously. This very short P-R conduction time would seem to confirm the existence of a much shorter conduction path than normal, just as is seen with a naturally occurring bundle of Kent.[55]

Comment

These experimental demonstrations and this first report of an apparent clinical surgical success in treating the medically relatively recalcitrant and incapacitating entity of complete heart block suggest a widespread applicability of such a surgical technique in individuals with this unfortunate complication. The actual surgical procedure performed is neither shocking nor physiologically burdensome. One would not expect to encounter significant operative mortality (Fig. 18).

CONCLUSIONS

1. The surgical procedures devised for the treatment of coronary arterial insufficiency may be classified according to the objectives they seek to accomplish.

2. Measures which modify only the clinical manifestations of the coronary arterial insufficiency consist of those which destroy the sympathetic pathways mediating pain sensation from the heart by postganglionic resection of the upper dorsal and lower cervical chains, by division of the preganglionic fibers to these same areas, or by paravertebral injections of alcohol.

3. The only available method which modifies the degree of coronary insufficiency by decreasing myocardial demand is destruction of thyroid function by surgical or medical therapy.

4. Coronary insufficiency may be decreased by a variety of procedures which are designed to increase the size of the coronary vascular bed. These are best termed revascularization techniques, and represent the most physiological approach to the problem. They are classified according to their ability to increase the vascularity at a superficial level or throughout all layers of the myocardium.

5. The blood supply to the epicardium, or the layers immediately beneath the epicardium, may be augmented by omentopexy, myopexy, pneumonopexy, the intrapericardial insufflation of irritants, or the implantation of the bleeding end of the mobilized left internal mammary artery into the left ventricular wall. The intrapericardial instillation of a powdered silicate appears to be the most promising of the *surface revascularization procedures.*

6. The term *total revascularization* is applied to the techniques which

create an anastomsis between the aorta and the coronary sinus either through a vascular graft (Beck II) or directly (Kralik modification) thus establishing a retrograde flow of arterial blood to the myocardial capillary bed by way of the venous channels. Such retrograde flow is transient but great augmentation of the adequacy of the intercoronary collateral system is produced and remains. Simple ligation of the coronary sinus also may be considered as a total revascularization procedure although a lesser degree of intercoronary overdevelopment is obtained by this procedure.

7. The selection of patients for the revascularization procedures is based upon those manifestations of the disease which indicate an ominous prognosis or seriously interfere with the ability of the patient to meet the requirements of ordinary living.

8. Resection of a ventricular aneurysm represents a promising surgical development in the management of a relatively recalcitrant and untoward cardiac complication which nearly always is the result of occlusive coronary arterial disease. The first historically successful case is herein presented.

9. The development of a seemingly satisfactory and rather safe surgical treatment for complete or varying heart block is detailed with presentation of the first apparently successful human operation.

CONCLUSIONES

1. Los procedimientos quirúrgicos ideados para el tratamiento de la insuficiencia coronaria pueden clasificarse de acuerdo con el fin que se propenen.

2. Son medidas que sólo modifican las manifestaciones clínicas de la insuficiencia coronaria, aquéllas que consisten en destruir las vías simpáticas aliviando la sensación dolorosa del corazón por medio de la resección postganglionar de las cadenas superior cervical e inferior cervical dividiendo las fibras preganglionares hacia estas áreas o bien por las inyecciones para vertebrales de alcohol.

3. El único método que existe para modificar el grado de la insuficiencia coronaria haciendo disminuir la demanda del miocardio, es la destrucción de la función tiroidea ya sea por procedimiento quirúrgico o médico.

4. La insuficiencia coronaria puede decrecer mediante varios procedimientos que tienden a aumentar el calibre de los vasos del lecho vascular coronario. Estos pueden mejor llamarse técnicas de revascularización y representan el modo más fisiológico de atacar el problema. Se clasifican de acuerdo con su aptitud para aumentar la vascularización en un plano superficial o a través de todas las capas del miocardio.

5. La provisión sanguínea al epicardio o a las capas inmediatamente debajo de él puede aumentarse por la omentopexia, la miopexia, neumopexia, la insuflación intrapericárdica de irritantes o la implantación del cabosangrante de la arteria mamaria interna movilizada dentro de la pared ventricular izquierda.

La aplicación intrapericárdica de un silicato en polvo parece ser el más prometedor de los métodos de revascularización superficial.

6. El término revascularización total se aplica a las técnicas que—crean anastomosis entre la aorta y el seno coronario por medio de un injerto vascular (Beck II) o bien directamente (Modificación de Kralik) estableciendo así un flujo retrógrado de sangre arterial hacia el lecho capilar del miocardio a través de las vías venosas. Tal flujo retrógrado es transitorio pero se produce un gran aumento de la eficacia del sistema colateral intercoronario y esto persiste. La simple ligadura del seno coronario también puede considerarse como un procedimiento de revascularización total-aunque menor grado de nuevo desarrollo intercoronario se obtiene por este método.

7. La selección de los enfermos para la revascularización se basa—sobre las manifestaciones de la enfermedad que indican un mal pronóstico o seria interferencia de la capacidad del enfermo para los requerimientos de la vida ordinaria.

8. La resección del aneurisma ventricular es una adquisición quirúrgica prometedora para el tratamiento de las complicaciones relativamente recalcitrantes que resultan casi siempre de la enfermedad coronaria oclusiva. El primer caso históricamente con éxito satisfactorio se presenta aqui.

9. El desarrollo de un procedimiento quirúrgico al parecer seguro para el bloqueo completo o variable del corazón se detalla con la presentación del primer caso humano aparentemente satisfactoriamente realizado.

RESUME

1. Les traitements chirurgicaux de l'insuffisance de l'artère coronaire peuvent être classés selon les objectifs qu'ils cherchent à atteindre.

2. Certains ne modifient que les manifestations cliniques de l'insuffisance de l'artère coronaire: ce sont ceux qui détruisent les trajets sympathiques transmettant la douleur venant du coeur. Il s'agit de la résection postganglionnaire des chaînes dorsales supérieures et cervicales inférieures, de la division des fibres préganglionnaires dans ces mêmes régions ou des alcoolisations paravertébrales.

3. Une seule méthode valable modifie le degré de l'insuffisance coronarienne en diminuant les besoins myocardiques: c'est la destruction de la fonction thyroïdienne par la chirurgie ou la thérapeutique médicamenteuse.

4. On peut diminuer l'insuffisance coronarienne par une série de procédés qui sont destinés à accroitre l'importance du lit vasculaire coronarien. Ce sont les procédés qui sont le plus exactement désignés sous le terme de moyens de revascularisation. Ils représentent la façon la plus physiologique d'aborder ces problèmes. Ils sont classés selon qu'ils sont susceptibles soit d'augmenter la vascularisation des plans strictement superficiels, soit d'atteindre toutes les couches du myocarde.

5. Le flux sanguin de l'épicarde, ou des couches immédiatement sous-jacentes peut être augmenté par l'omentopexie, la myopexie, la pneumopexie, l'insufflation intrapéricardique de substances irritantes, ou l'implantation de l'extrémité saignante de l'artère mammaire interne gauche dans la paroi du ventricule gauche.

L'instillation péricardique de silicate en poudre semble être le procédé de revascularization superficielle le plus satisfaisant.

6. Le terme "revascularisation totale" est appliqué aux procédés qui créent une anastomose entre l'aorte et le sinus coronaire, soit par greffe vasculaire (Beck II) soit directement en établissant un courant rétrograde de sang artériel vers le lit capillaire myocardique par les conduits veineux. Un tel courant rétrograde est passager, mais il produit une grande augmentation de l'importance du système collatéral intercoronarien qui persiste. La simple ligature du sinus coronaire peut aussi être considérée comme un procédé de revascularisation totale, bien qu'il donne un plus faible degré de développement intercoronarien.

7. Le choix des malades pour le procédé de revascularisation est fondé sur l'existence de manifestations telles qu'elles laissent supposer un pronostic sérieux, ou qu'elles empêchent manifestement le malade de mener une vie normale.

8. La résection d'un anévrysme ventriculaire reprèsente un progrès chirurgical plein de promesse pour obtenir la guérison d'une complication cardiaque relativement récalcitrante et insurmontable, qui presque toujours provient de la thrombose de l'artère coronaire. Les auteurs rapportent le premier cas historiquement traité avec succès.

9. Ils exposent en détail le développement d'un traitement chirurgical également satisfaisant et sans risque syndrome d'Adams-Stokes complet ou partiel, avec présentation d'un cas qui semble avoir été opéré avec succès.

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Clinical and Physiological Studies on the Use of Metacortandracin* in Respiratory Disease

I. Bronchial Asthma

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In the report of Bunim et al[1] the use of metacortandralone and metacortandracin in rheumatoid arthritis was found to be accompanied by marked symptomatic benefit but without producing retention of sodium or loss of potassium as observed in cases treated with cortisone, hydrocortisone or ACTH. The purpose of this investigation was to study the effects of the administration of metacortandracin in patients suffering from respiratory disease, including especially bronchial asthma, presented in Part I, and pulmonary emphysema and pulmonary fibrosis, in Part II.*** In some of these cases, bronchiectasis, chronic bronchitis and varying degrees of cardiac insufficiency were also present. The changes in clinical response were correlated in many instances with measurements of respiratory function.

Methods

Metacortandracin was administered in four divided doses daily, generally at meal time and between 11 and 12 p.m. In patients with intractable bronchospasm a dosage of 60 to 80 mg. a day was employed for one to two days, 40 to 60 mg. per day for three to four days and 10 to 30 mg. daily thereafter, depending on the response of the patient. In cases in which a maintenance dosage of 60 to 100 mg. of hydrocortisone had previously been used, the dosage of metacortandracin varied between 20 and 40 mg. a day. The response to treatment with either cortisone, hydrocortisone or ACTH was known in 18 of the 30 patients in this series. The age, sex distribution and dosage schedule is illustrated in Table I

TABLE I

AGE, SEX DISTRIBUTION AND AVERAGE DOSAGE OF METACORTANDRACIN IN 30 PATIENTS WITH BRONCHIAL ASTHMA

Age (yrs.)		Sex		Average Daily Dosage (mgs.) Initial		Maintenance	
Mean	Range	Male	Female	First Day	First Week	Mgs./Day	No. of Days
49.5	14-72	16	14	50	35	15	16.4

The measurement of the respiratory function included the vital capacity, performed with a gradual expiration, and also with a swift or forceful expiration. In another study from this clinic[2] it was shown that the

*Metacortandracin (Metacortin) used in this study and furnished by Schering Corporation, Bloomfield, New Jersey has been re-named Prednisone.

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***Part II will be published in an early issue of Diseases of The Chest.

maximal and, therefore, the true vital capacity was only obtained by a relatively slow, non-forceful expiration since, in some patients with bronchial asthma and the majority of those with either functional or organic pulmonary emphysema, the use of a rapid, forceful or vigorous effort to expel the inhaled atmosphere produced a premature closure of the smaller bronchi, with a vital capacity frequently 50 per cent lower than the measurement recorded with a non-forceful effort. The vital capacity when described as such refers to a gradual, non-forceful expiration; a fast expiration should not be considered to represent the patient's actual lung vital capacity but rather the current of air that is expelled by this maneuver, which reveals air-trapping, as in emphysema of the lungs.

The determination of the pulmonary ventilation with inhalation of air and 100 per cent oxygen was employed to reveal impairment of diffusion of oxygen, since our studies had shown that the air-oxygen ventilatory difference was often marked in pulmonary emphysema and, furthermore, could be used in many cases as a test that quantitatively recorded, these patients capacity for exercise.[3] The maximal breathing capacity (M.B.C.) was measured in some instances; this test was of value in portraying ventilatory difficulties due to bronchial asthma. When pulmonary emphysema was also present, it often revealed little more than the comparison between the vital capacity and a forceful expiration or fast "vital capacity." Since the trapping of air from alveolar overdistension which often is a result of the M.B.C. test produces an augmentation of dyspnea, we do not now routinely employ it in cases of pulmonary emphysema.

The weight and blood pressure were recorded daily in hospitalized patients, and once or twice a week in ambulatory patients.

Results

The relief of bronchospasm accomplished by metacortandracin was found to be similar to that achieved by cortisone, hydrocortisone and ACTH, with the exception that a more prompt response to this drug was at times observed than with the previously used steroids studied under similar circumstances.[4] The onset of subjective benefit, recorded in Figure 1, took place within 24 to 48 hours in 25 of 30 cases. It became evident later by comparative studies that in patients with intractable asthma a larger initial dosage (60 to 80 mg. daily) for the first several days was more apt to initiate an early remission. A marked subjective improvement accompanied by disappearance of sibilant rales was recorded an excellent response. Moderate improvement included substantial relief of dyspnea and a decrease in sibilant rales in the lungs. Lack of benefit occurred in only one patient with bronchial asthma in whom apparent addiction to demerol was present.

Seventeen of the 30 patients in this series responded with a complete remission, as seen in Table II. Eleven of these had been on maintenance therapy with hydrocortisone prior to administering metacortandracin; their symptoms had been only partially controlled on dosages of hydrocortisone between 60 and 120 mg. daily. In 10 of these 11 subjects more

TABLE II
CLINICAL IMPROVEMENT RESULTING FROM THE USE OF METACORTANDRACIN IN BRONCHIAL ASTHMA

No. of Cases	Mean Onset of Improvement (hrs.)	Remissions Complete	Remissions Partial	None
30	40	17	12	1

freedom from asthmatic symptoms was obtained by maintenance therapy with dosage levels of 10 to 20 mg. daily over a period of one to two months.

Twelve patients, or 40 per cent of the total, had moderate benefit, which was considered a partial remission. Six of these had received maintenance hydrocortisone therapy. The clinical response to metacortandracin was qualitatively similar to that obtained with a hydrocortisone dosage four to five times higher. One patient with chronic intractable asthma who had been hospitalized for the past 12 years had little or no response to metacortandracin. This patient was resistant to bronchodilator agents and had received no benefit from denervation of the posterior pulmonary plexi. Demerol afforded relief and her apparent addiction to this drug made any evaluation of metacortandracin difficult.

Ventilatory function studies performed before and 4 to 7 days after onset of metacortandracin therapy when maximal benefit had been obtained revealed a marked improvement in both the vital capacity and in

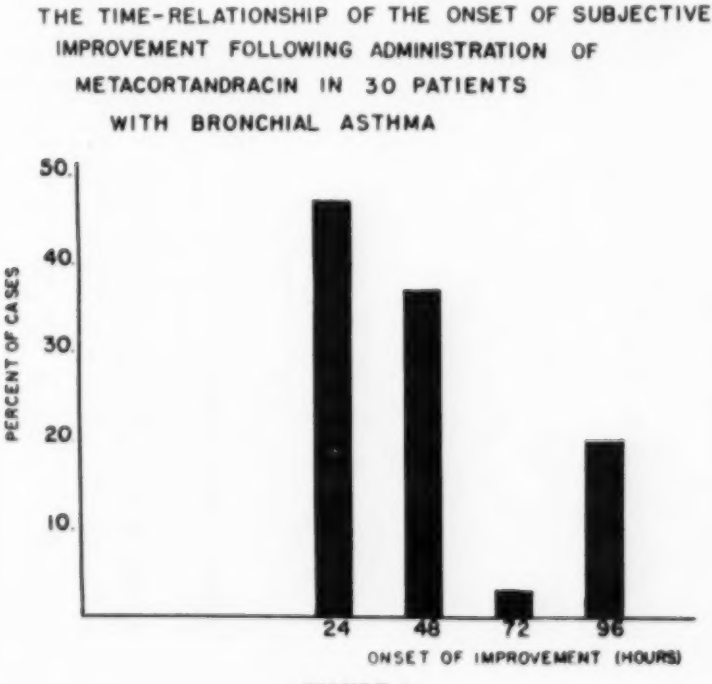

FIGURE 1

the fast expiration volume of the 21 patients tested. The mean per cent change in the vital capacity was 53.2 per cent, and in the fast expiration 60.6 per cent. These data are represented graphically in Figure 2. The maximal breathing capacity after metacortandracin revealed a mean change of 44.5 per cent in the 8 patients tested, as charted in Figure 3. Three of the four patients who showed insignificant changes in maximal

TABLE III

Pulmonary Function Test	Before	After
Vital Capacity (cc.)	1,900	3,200
Maximal Breathing Capacity (cc. per min.)	34,200	58,800
Pulmonary Ventilation (cc. per min.)		
Breathing Air	9,500	7,600
Breathing Oxygen	8,400	5,700
Oxygen Consumption (cc. per min.)		
Breathing Air	349	256

Increase in Vital Capacity and Maximal Breathing Capacity, with decrease in Pulmonary Ventiliation and Oxygen Consumption in a patient with Bronchial Asthma after 2 weeks of metacortandracin therapy.

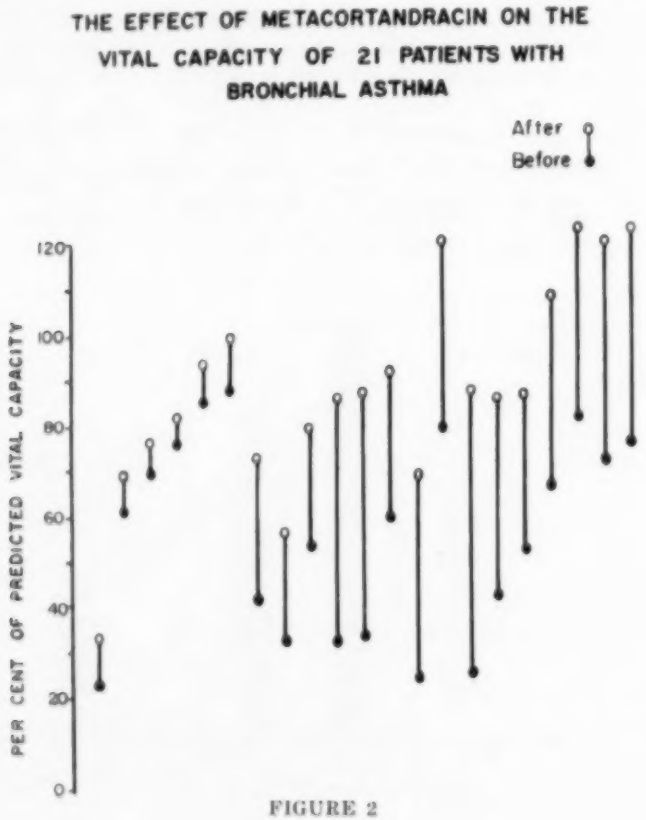

FIGURE 2

breathing capacity after therapy had been receiving maintenance hydrocortisone prior to the initial test. A more detailed summary of the ventilatory function studies in Case 1 is illustrated in Table III. Spirographic tracings of the increase in vital capacity and M.B.C. are shown in Figures 4 and 5.

In patients with bronchial asthma without cardiac insufficiency a remission was obtained without the use of salt restriction or additional ingestion of potassium chloride. The clinical evaluation of *short-term* therapy was not different from that previously accomplished with hydrocortisone except that the opportunity of adding salt to a regular diet added to the patient's sense of well-being. However, in longer treatment, such as three to six weeks of metacortandracin therapy, a significant finding was the decrease or disappearance of a moon-like swollen appearance to the face in 6 patients who had been on hydrocortisone for six months or more. In two of these cases, girdle adiposity was diminished. In 5 patients previously on maintenance therapy with hydrocortisone an average weight loss of 6 pounds took place at the end of one week's treatment with metacortandracin, This response suggests a mobilization and excretion of extracellular fluid rather than increased tissue catabolism although these were not measured.

The side effects encountered in our study included (1) a reddening of the palmar surface of the hands in one case, (2) headache in three cases. In one patient the headache appeared twenty minutes after taking the

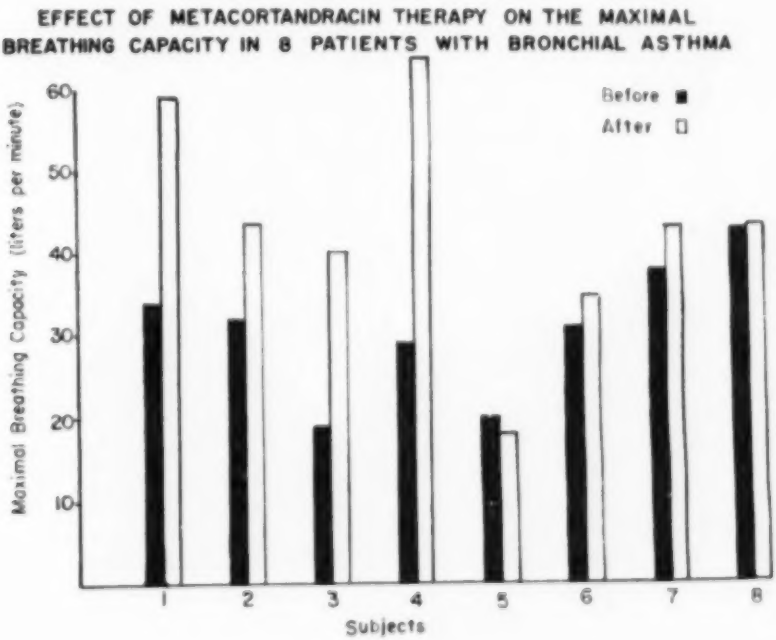

FIGURE 3

drug for a period of one week, then gradually disappeared in two weeks, without recurrence on subsequent maintenance therapy with 15 mg. daily for two months. In two other patients in whom headache had previously occurred during the administration of hydrocortisone, a similar headache was provoked by metacortandracin. In one of these cases in which the dosage was reduced to 5 mg. per day the headache disappeared. (3) Dizziness was occasionally noted in three patients. (4) The occurrence of undue stimulation was encountered in one case in which a similar but more marked reaction to hydrocortisone had been noted. However, in other patients in whom cortisone had previously produced a noticeable degree of a heightened awareness toward life, feeling of stimulation or a marked elevation in mood, a similar response was observed at times with employment of metacortandracin but generally of less marked degree. (5) In three patients abdominal distress, which had been observed after treatment with hydrocortisone included either pain after eating or a sensation of fullness. In one who had previously had a duodenal ulcer, x-ray of the gastrointestinal tract was negative after six months treatment with hydrocortisone and three weeks with metacortandracin. The complaints of these patients appeared to be aided by temporary administration of aluminum hydroxide.

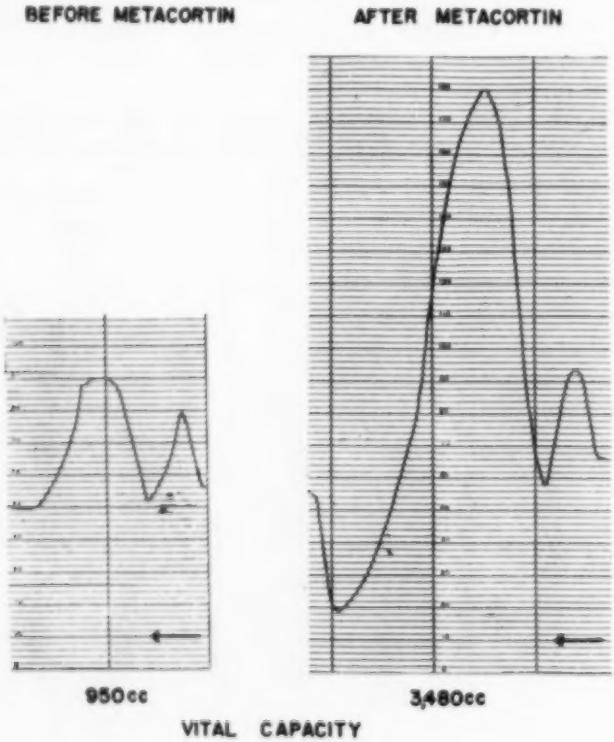

FIGURE 4

In patients with an associated bronchiectasis control of infection should be attempted by appropriate antibiotic therapy and by effective bronchial drainage. Since the development of exsufflation with negative pressure, and the two apparatus we have described*,[6, 7] it has become apparent that elimination of retained secretions is more efficiently accomplished with the higher expiratory flow rates obtained by negative pressures of 40 mm Hg. In a number of instances, the use of E.W:N:P. has facilitated adequate control of infection, at home as well as in the hospital.

Illustrative case reports follow:

Case 1, male, age 55 years. Diagnosis: Bronchial asthma. Past history: Bronchial asthma for 20 years, increasing in severity during past five years, despite hypo-sensitization dust and vaccine therapy.

During the two years prior to treatment asthmatic dyspnea had been poorly controlled by daily administration of 40 to 50 mg. ACTH or by hydrocortisone 100 mg. daily, when substituted for ACTH. Fever therapy with Kirk's typhoid vaccine was given at weekly to two week intervals during the previous six months to aid in the

*The apparatus referred to are the Eliott Medical Plastics Exsufflator and the O.E.M. Cof-flator.

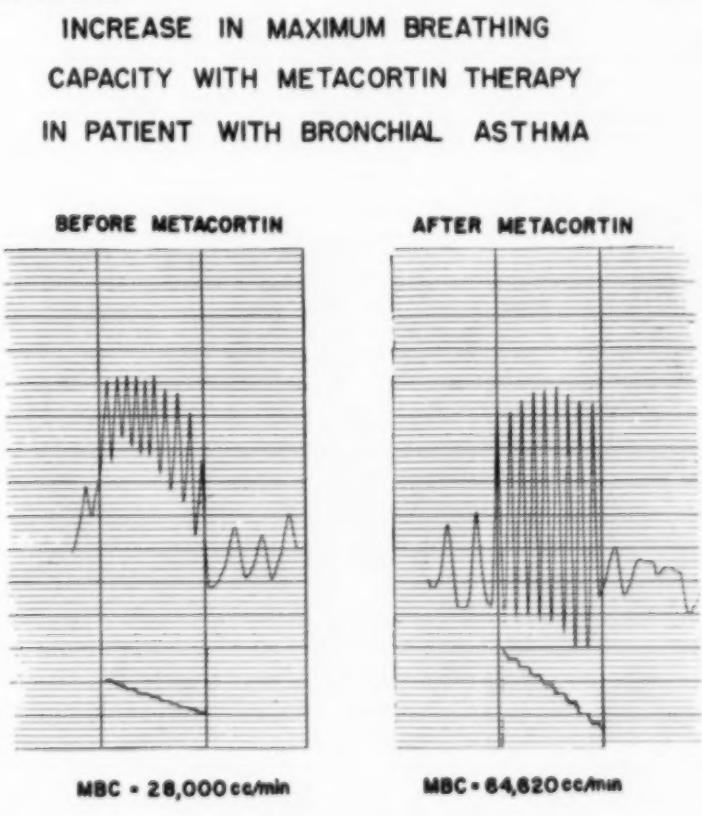

FIGURE 5

response to either ACTH or hydrocortisone. In addition, the Vaponefrin nebulizer was employed, generally with the administration of 2.25 per cent racemic epinephrine (Vaponefrin), at times with Isuprel 1 per cent, or with a mixture of racemic epinephrine and atropine (Dylephrin). Broncho-dilator medication was taken in the form of aminophylline 0.35 gm. twice daily (Cardalin). Potassium iodide was generally taken, and, for occasional two week periods, a mixture of iodides and Fowler's solution. Dyspnea was present on slight or moderate exertion.

Physical examination during this period almost always revealed the presence of numerous sibilant rales. Diagnosis of intrinsic bronchial asthma was made.

The administration of metacortandracin in a dosage of 30 mg. a day for one week resulted in complete clearing of asthma, without sibilant rales in the chest. The initial improvement was noted at the end of 48 hours. On subsequent attempts to lower the dosage to 15 mg. per day, asthma of moderate severity recurred. However, a maintenance dosage of 25 mg. a day was accompanied by substantial relief of asthma, with a consequent markedly lessened need of other broncho-dilator medication. The face, which had manifested a round, swollen outline, now revealed the facial markings more distinctly. The response in this patient was gratifying indeed since the capacity to eat a regular diet, including steaks and salted food, appeared to be followed by improvement in strength and general well being and an ability to practice medicine more effectively than previously. The patient has been continuously treated since November 26th, 1954. In the accompanying Table II, the improvement in vital capacity and M.B.C. are revealed. Maintenance therapy continues as of April 1.

The increase in maximal minute ventilation portrays the decrease in the amount of bronchospasm accomplished by the use of metacortandracin in an individual who had previously been on a considerable dosage of either ACTH gel or hydrocortisone. In this patient, maintenance therapy requires 30 mg. per day at the present time to prevent recurrence of asthmatic dyspnea at night. It is of considerable interest to observe that the pulmonary ventilation breathing air was decreased from 9550 to 7650 cc. per minute under similar although non-basal conditions in office visit tests. However, the decrease in the ventilation when 100 per cent oxygen was substituted for air both before and after treatment revealed that, in addition to the presence of bronchial asthma, this patient has sufficient pulmonary emphysema as to result in impairment of diffusion of oxygen, manifestly revealed during the inhalation of pure oxygen. The manifestations of pulmonary emphysema by x-ray can be discerned, but they are relatively slight.

Case 2, female, age 51 years. R. J., with history of bronchial asthma and probable periarteritis nodosa of 7 years duration, was admitted to Presbyterian Hospital on November 26, 1954 because of recurrence of severe dyspnea, cough productive of purulent sputum and swelling of the abdomen. She had been treated almost continuously with ACTH, cortisone and hydrocortisone for the previous three years. A decrease of response of patient's asthma to this medication had occurred since the summer of 1953. A daily maintenance dose of 80 mg. hydrocortisone just before admission did not prevent increasing dyspnea necessitating hospitalization. She was placed on 60 mg. of metacortandracin on the day of admission followed by 30 mg. daily. Within 24 hours marked reduction in asthma occurred, and after 2 days bronchospasm and dyspnea had disappeared. A weight loss of 4 lbs. occurred within 3 days. Because of the findings of a large pelvic mass an operation was scheduled for December 4, 1954. Preoperative administration of a test dose of ACTH revealed marked suppression of adrenocortical function. She was maintained on 30 mg. metacortin up to the time of operation without recurrence of bronchospasm. Because of the unavailability of parenteral metacortandracin a total of 400 mg. of hydrocortisone was administered parenterally on the day of operation. This was discontinued on the day after operation and metacortandracin 40 mg. daily was administered for 3 days and then reduced to 25 mg. for 6 days. Maintenance was achieved with 15 mg. and later 10 mg. daily for a period of 2 weeks. Because of increasing dyspnea the daily maintenance dose of metacortandracin was increased to 25 mg. daily. She has had no recurrence of bronchial infection. Maintenance therapy continues as of April 1.

Case 3, female, age 38. Severe bronchial asthma of 9 years duration was accompanied by bronchiectasis of the right middle lobe. Treatment with fever therapy, parasympathetic denervation of both lungs, right middle lobe resection had no discernible effect on a state of intermittently recurring severe asthma. ACTH, cortisone and hydrocortisone were administered to establish remissions since August, 1952. The maintenance dose of hydrocortisone was gradually increased to 60 to 80 mg. per day with partial control of bronchospasm, although severe headaches appeared to result from its use. Rounding of the face, a marked increase in the supra-mammary fat pads and a buffalo hump appeared. Hypertension of 170/100 was present.

When she was placed on metacortandracin 30 mg. daily, a marked reduction of asthma was noted in 24 hours; and at the end of four days, she was put on 15 mg. daily. The headaches persisted while on the drug. A vital capacity, taken before

metacortandracin was begun, was 1.2 liters. Following a single injection of 375 mg. of diphenmethanil methysulfate* the vital capacity rose to 3.2 liters and marked elimination in bronchospasm was noted. After a week's course of metacortandracin the vital capacity was 2.8 liters before and 3.2 liters after 1.5 cc. diphenmethanil methysulfate. When metacortandracin was discontinued for 48 hours, after a course lasting for 26 days, and hydrocortisone, 60 mg. daily, was substituted, an exacerbation of asthma occurred. Metacortandracin has been used continuously since then, at a dosage that varies between 10 and 15 mg. daily. Headaches are still present intermittently, but less severe. Her facial roundness is somewhat diminished. Maintenance therapy continues as of April 1.

Case 4, male, age 72 years, diagnosis: Bronchial asthma, cardiac insufficiency, chronic sinusitis. Shortness of breath accompanied by wheezing and cough began seven years ago. Stuffiness of the nose had been present intermittently for thirty years prior to the development of bronchial asthma. Four years ago a hyposensitization program was initiated with injection of dust, ragweed and alternaria. Since that time the patient has had episodes of acute supperative sinusitis involving the left antrum and ethmoid which have generally precipitated increased severity of bronchial asthma until the infectious process was controlled. During the past four years the patient was given cortisone or hydrocortisone for periods of ten days to three weeks on twelve separate occasions. During the last course in the month of November, 1954, he developed edema of the ankles, a weight gain of seven pounds and a 2 cm. enlargement of the transverse diameter of the heart. Although he had been as careful in restricting salt intake as he was during previous periods of hydrocortisone treatment, he manifested signs of cardiac insufficiency at this time. On treatment with digitalis, mercuhydrin, and diamox, his weight decreased ten pounds in a period of one month.

Increasingly severe asthma then began again without obvious cause. On January 10, 1955, metacortandracin was begun at a dosage of 60 mg. daily. Substantial relief of dyspnea, noted in 48 hours, became more complete two days later. The dosage of metacortandracin was reduced to 30 mg. a day for a period of four days, 20 mg. for four days, 10 mg. daily for two weeks, and 5 mg. daily at breakfast since then to February 28, 1955. During the first weeks of treatment with metacortandracin the patient lost an additional four pounds. The cardiac enlargement noted previously as a result of administration of hydrocortisone had receded prior to treatment with metacortandracin, as a result of digitalization and diuretic therapy. No increase in heart size was observed during the treatment with metacortandracin. Diamox,, 250 mg. is administered once weekly. Maintenance therapy continues as of April 1.

If treatment with hydrocortisone had been used during the last episode of asthma, it would have been undertaken with some trepidation and, in any event, with considerable caution since the previous course resulted in overt symptoms of insufficiency. No etiology for disease of the heart was evident. The assumption of arteriosclerotic heart disease was made because of his age since the blood pressure was normal and there were no significant changes in the electrocardiogram. The advantage of employing a steroid hormone that did not precipitate cardiac failure was obvious since a salt retaining effect was not produced.

Comments

Although the long-term effects of treatment with metacortandracin are not now available, the advantage of this drug over cortisone and hydrocortisone have been clearly revealed in this series of patients with bronchial asthma.

The response to administration of metacortandracin in terms of relief of bronchospasm is qualitatively similar to that induced by hydrocortisone. Relief from dyspnea generally sets in between the first and fourth day of treatment, depending upon the intractable nature of the patient's asthma and the dosage of steroid hormone used. In other respects, the advantages of metacortandracin became evident. The patients in whom the use of cortisone had previously resulted in leg or sacral edema, mooning of the face or cardiac enlargement, despite the patient's attempts to eat a prescribed low salt diet, the substitution of metacortandracin for hydrocortisone in a dosage which provided equal or even greater complete relief of bronchospasm was uniformly follow by diminution or disappear-

*Dispensed as *prantal* by Schering Corporation.

ance of these complications. In addition, no need existed for supplementary use of 3 to 5 gm. of potassium chloride daily, which was found to be a highly desirable part of the program for administration of cortisone or hydrocortisone in the studies of Kinsell[3] as well as ourselves,[4] as was originally pointed out in the use of metacortandracin in arthritis by Bunim et al.[1] In our previous experience with patients treated with cortisone or hydrocortisone, when the development of edema required employment of mercuhydrin, a diuresis often precipitated weakness and malaise in patients who had not been supplied with additional potassium chloride.

In cases that had required a maintenance dosage of 60 to 80 mg. of hydrocortisone a day, the metacortandracin dosage was usually between a range of 10 to 30 mg. daily, with either an almost complete disappearance or a marked lessening of asthma and a lesser requirement for bronchodilator aerosols and similar oral medication.

In the cases that had been on maintenance therapy with hydrocortisone the substitution of metacortandracin was generally accompanied by more marked clinical betterment both in respect to the control of bronchospasm as well as feelings of well-being. Nevertheless, no instances of abnormal euphoria were encountered. In the patients without overt or latent cardiac insufficiency the privilege of using a regular diet with as much salt as desired was conspicuously gratifying. In two cases characterized by bronchial asthma with productive allergic expectoration, the administration of 20 mg. daily provided no improvement beyond that obtained by maintenance treatment with 80 mg. hydrocortisone. In these cases, a higher dosage of metacortandracin was apparently required for a better effect.

The determination of maintenance dosage of metacortandracin is dependent upon the degree of freedom from bronchospasm desired by both the patient and the physician. In our previous use of adrenocortical hormones, attempts were frequently made to stop the use of these drugs or to lower the dosage to that which seemed the minimal effective dosage. Patients were encouraged to employ conventional measures to aid in the relief of asthmatic dyspnea, including nebulized epinephrine preparations and mixtures of aminophylline and ephedrine by mouth, as well as a semi-continuous use of potassium iodide and other agents employed from time to time in the attempt to obtain a remission in the symptoms of asthma. These considerations, to our mind, apply to the use of metacortandracin although the complications due to disturbance in the sodium and potassium salts did not take place with the dosage used in our cases. In the presence of a history of duodenal or gastric ulcer, steroid hormones are obviously a hazard. Although a patient who had had a duodenal ulcer was treated with metacortandracin and x-ray taken 3 weeks later was negative, it would seem to be a good precaution to employ aluminum hydroxide, plenty of milk and perhaps also one of the anti-cholinergic drugs routinely if there are complaints of indigestion or pain after meals.

In 25 additional cases not reported in this series, three instances of

bronchial infection appeared during metacortandracin therapy; otherwise the clinical results were similar.

SUMMARY

A preliminary report on the use of metacortandracin in 30 patients with bronchial asthma is presented. The clinical findings of short term therapy with this steroid include: (1) disappearance or relief of bronchospasm and asthmatic dyspnea in 29 instances; (2) the capacity to eat a regular diet with added salt and without the use of supplementary feeding of potassium in patients without heart disease, in contrast to the need for a salt poor diet and potassium administration with the administration of cortisone, hydrocortisone and ACTH; (3) in 5 patients previously on maintenance therapy with hydrocortisone, the substitution of metacortandracin for hydrocortisone resulted in average weight loss of 6 pounds occurring in a period of one week. In 6 patients mooning of the face became much less prominent. (4) The subjective effect of eating a regular diet in the cases without cardiac failure was a happy one. (5) The side effects were slight, resembling, but to a lesser extent those seen with cortisone treatment, i. e., mental stimulation, abdominal discomfort, occasional headache and transient dizziness.

Respiratory function test confirmed the clinical impression of decrease or disappearance of bronchospasm.

Although further studies are required to supplement the findings of this preliminary investigation, it seems to the authors that this new steroid hormone is a drug of considerable value in the treatment of intractable bronchial asthma. Furthermore, in cases of persistent asthmatic dyspnea with an associated cardiac insufficiency, the safety of administering metacortandracin, in contrast to cortisone, became evident. The effect of this drug in lowering resistance to infection requires further study.

The long term evaluation of this steroid is not possible at this time, but it is to be emphasized that all of the side effects of cortisone, except for salt and water retention, at moderate dosages used, have already been observed. What their significance may be in the protracted management of certain bronchopulmonary disorders obviously cannot be stated at this time.

RESUMEN

Se presenta una información preliminar sobre el uso de metacortandracina en 30 enfermos con asma bronquial. Los hallazgos clínicos después del tratamiento a corto plazo con este esteroide comprenden: (1) Desaparición o alivio del broncoespasmo y la disnea asmática en 29 casos: (2) la capacidad para ingerir una alimentación normal con sal y sin proporcionar potasio adicional en enfermos sin afección-cardiaca en contraste con la necesidad de dar una dieta pobre en sal y la de dar potasio cuando se usa cortisona y ACTH; (3) en cinco que antes se sostenían con tratamiento de hidrocortisona, la substitución por metacortandracina produjo una pérdida de peso medio de 6 libras en una semana. En seis enfermos la apariencia lunar de la carase hizo mucho menos notable. (4) El efecto

subjetivo de comer una-dieta normal en los no cardiacos fué feliz. (5) Los efectos colaterales son ligeros, semejantes pero en menor escala a los de la cortisona como el estímulo mental, molestias abdominales, cefálea ocasional y mareo transitorio.

El estudio de la función respiratoria confirmó la impresión clínica de decrecimiento a desaparición del broncoespasmo.

Aunque se requieren ulteriores estudios para completar los hallazgos de esta investigación preliminar, les parece a los autores-que esta nueva hormona esteroide es una droga de considerable valor en el tratamiento del asma rebelde. Más aún, en casos de disnea asmática persistente con insuficiencia cardiaca asociada la seguridad al administrar metacortandracina, en lugar de cortisona, se hizo evidente. El efecto de est droga disminuyendo la resistencia a la infección, requiere más estudio.

Hasta ahora, la estimación del valor de este esteroide a largo plazo obviamente no es posible pero es de notarse que todos los-efectos colaterales de la cortisona con excepción de la retención de agua y sal se han observado. No puede aún determinarse cuál es su-significación en el tratamiento prolongado de ciertos trastornos-broncoespasmódicos.

RESUME

Les auteurs présentent un rapport préliminaire sur l'utilisation de la "métacortandracine" chez 30 malades atteints d'asthme bronchique. Les constatations cliniques d'un traitement de courte durée par ce stéroïde sont les suivantes:

1) Disparition ou soulagement du bronchospasme et de la dyspnée asthmatique dans 29 cas.

2) Possibilité de garder un régime alimentaire normal avec sel et sans ingestion supplémentaire de potassium chez les malades indemnes d'affections cardiaques, au contraire de ce qui se passe quand il s'agit de l'administration de cortisone, d'hydrocortisone, ou d'A.C.T.H. qui nécessite le régime désodé et additionné de potassium.

3) Chez cinq malades, primitivement soumis à un traitement continu par l'hydrocortisone, son remplacement par la "métacortandracine" amena une perte de poids de six livres en moyenne, pour une période d'une semaine. Chez six malades, l'aspect bouffi du visage devint moins net.

4) L'effet psychologique d'une alimentation normale chez les malades indemnes de troubles cardiaques fut très heureux.

5) Les effets secondaires furent très légers, ressemblant, mais à un moindre degré, à ceux que l'on peut voir au cours du traitement par la cortisone: excitation mentale, troubles abdominaux, migraines parfois et nausée passagère.

L'étude de la fonction respiratoire confirma l'impression clinique d'une diminution ou de la disparition du bronchospasme.

Bien que des études ultérieures soient nécessaires pour compléter ces recherches préliminaires, il semble aux auteurs que cette nouvelle hormone stéroïde a une valeur considérable dans le traitement des asthmes bronchiques incurables. De plus, dans les cas d'état de mal asthmatique, avec insuffisance cardiaque, l'administration de la "métacortandracine" est

d'une bénignité manifeste, au contraire de la cortisone. L'effet de ce produit sur la diminution de la résistance à l'infection demande des étude ultérieures.

Il n'est pas possible pour le moment d'avoir un recul suffisant pour évaluer l'action de ce stéroïde. Toutefois, il faut insister sur le fait qu'il peut provoquer, aux doses, faibles qui ont été utilisées, tous les effets secondaires de la cortisone, à l'exception de la rétention hydrique et chloruré sodique. On n'a évidemment pas encore pu constater quelles seront leurs conséquences au cours du traitement prolongé de certains troubles broncho-pulmonaires.

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The State Care of the Tuberculous in Colorado through the Use of Existing Facilities*

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Brief History

Colorado has been a Mecca for many years for health seekers, especially those with tuberculosis, and though many attempts had been made by the Colorado Tuberculosis Association to provide some care for the indigent tuberculosis sufferer in our midst, these efforts had met with no success until 1937.

FINALLY, in 1936, an Initiated Act was voted by the people providing $50,000 a year to be spent for the indigent tuberculous. The Act was drawn up by the Colorado Tuberculosis Association and the spending of this money was placed under the Colorado State Department of Welfare for administration.

The Plan and How It Works

The law provided for a full-time director; the position was placed under Civil Service and the qualifications for the position provided that the director should be a physician with at least five years' experience in chest diseases, chiefly tuberculosis. The Director is given the full responsibility for the functioning of the Division and is directly responsible to the Colorado State Board of Public Welfare and reports to the board every month at their regular monthly meeting regarding the progress of his division.

Individuals afflicted with tuberculosis who are no longer able to pay for their care may apply to the County Welfare Department of the county in which they reside for aid. They sign an application requesting this aid. The law provides that:

(1) They must have one year of state residence unless they are under one year of age. The original law stated that three years of residency was necessary.

(2) They must be medically indigent. The County Welfare Department investigates the residency and need and signs an agreement to pay 50 per cent of the total cost of care. The application is then sent to the office of the director of tuberculosis hospitalization at the state capitol with a brief medical form filled out by a physician. This includes a sputum report and, in case of children, a report of the tuberculin test. Recent chest x-ray films are also required. The case, after study, is then approved or denied; and if approved it is sent to one of 11 different institutions by the director. These are described later in the paper.

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In general, a location nearest the patient's home and also his religious affiliation are considered when placing the individual. Difficult diagnostic problems and cases that are considered candidates for surgery who have already had prolonged drug therapy are sent to Colorado General Hospital.

This whole process from application to the time that the patient enters the hospital or sanatorium now takes an average of 18 days. Emergencies are hospitalized within 12 hours by the counties pending state acceptance. Fifty per cent of the bill is reimbursed by the state and the Division of Tuberculosis Hospitalization supervises the care that the patient receives by means of frequent reviews with the staffs of the institutions in which the patients are hospitalized. These reviews range in frequency from once a week for cases at the Colorado General Hospital to once in two months for two of the smaller institutions, one of which is the farthest removed from headquarters in Denver. Reviews are made by a team composed of the director, one of the chest surgical consultants (who is also one of the four surgeons responsible for our chest surgery at Colorado General Hospital), a medical social worker (attached to our Division, except in the case of institutions that have their own medical social worker), usually an occupational therapy worker and, frequently, a rehabilitation consultant. *I cannot overemphasize the importance of this periodic review.* Before these reviews were started there was a great deal of variation between the type of care received by patients in different institutions. Also, those in some institutions felt lost or neglected.

What Hospitals and Sanatoria Are Used?

The institution must be licensed by the State Department of Public Health for the care of tuberculosis and that Department has set up certain, rather comprehensive rules and regulations with which institutions must comply before they are eligible for licensing. Furthermore, they must be approved by the Colorado State Board of Public Welfare on the recommendation of the Director of the Division of Tuberculosis Hospitalization for the care of our State patients. *No beds are under contract.* All institutions, except four, receive the same basic rate per day which is $6.50 at the present time for nursing care ($6.60 if both medical social and occupational therapy service is provided). In addition to this basic rate x-ray films, drugs and laboratory procedures are paid for according to a list of charges which have been approved by the Colorado State Board of Public Welfare and these payments are uniform for all institutions. Drugs are paid for at cost to the institution plus 10 per cent for overhead. The charges for specialized services, like physiotherapy following surgery, EKG, etc., are, as a rule, about 50 per cent of the usual charges made to private patients. This applies to special x-ray studies like gastrointestinal series, planigrams, etc. The physician at the institution who is in charge of the day-to-day care must be one who has had special training in tuberculosis work and be acceptable to both the institution and the director of the Division of Tuberculosis Hospitalization. Usually the di-

rector chooses between two or three physicians nominated for the position by the institution and the patient is placed under his continued care. This is something the patients like very much in contrast to the frequent changing of doctors as is the case in so many state and veterans' hospitals. Payment is made to him of $15 per month per case. Two institutions giving ambulant care are paid $4.50 a day ($4.60 if medical social and occupational therapy services are also given) and they are paid in addition, according to the schedule of approved charges mentioned above for other procedures.

A guide booklet giving uniform rules and regulations, and accepted by all the institutions we use, has been worked out and published by the Colorado State Tuberculosis Association and a copy is given each patient on admission. This is valuable in providing for uniformity of rules and regulations and exercise gradations between institutions so that transfer of patients can be made with a minimum of confusion.

An institution has the right to refuse hospitalization or to discharge any patient for violation of rules and regulations. We usually ask that the patient be given a second chance and that is usually granted except in cases of flagrant violation. Actually, acceptance of our cases usually does not present much, if any, problem. A social history of every state patient is sent the physician by our Social Service Department before the patient arrives. In this way the doctor and the institution is forewarned in the case of problems. Almost every case, even convicts on parole, ex-convicts, alcoholics and borderline psychotics are accepted and given a trial, not only in one, but several institutions before we throw up our hands and regard the case as unmanageable. Few individuals, therefore, fall into this hopeless category and this only after patient trial and some degree of treatment has been achieved. We reserve the right to remove the patient from an institution at any time, and it is understood that before discharge of the patient from an institution consultation will be had with the director of the Division of Tuberculosis Hospitalization.

Ancillary Services Given Patients

I have already mentioned that the medical condition of every patient is reviewed once in two months—in many instances once a month—with the staff of the institution in which the patient is placed. These conferences are usually stimulating to all concerned and everyone interested in the progress of the patient has a chance to make suggestions that may be helpful. There is no attempt on our part to "tell" the staff how the case should be handled. It is more a meeting of minds and an attempt to secure uniformity of care between institutions. I find that the staffs of the institutions welcome these reviews at regular intervals and patients are given the justified feeling that there is an interest on the part of many in their progress. All receive occupational therapy, a chance for vocational rehabilitation if, in medical opinion, it seems advisable for the individual not to return to his former occupation. Also, and this is most

important—he has medical social consultation either furnished by a qualified medical social worker on the staff of the sanatorium or, if the hospital or sanatorium does not have such a worker, by one of the medical social consultants on my staff.

We have reaped a number of benefits from this service. Doctors in the sanatoria have recognized that the social worker is a person who will listen patiently to the problems and complaints of the patients. They are excellent "trouble-shooters." The doctors have learned, too, that in the day-by-day contact of the social worker with the patient she comes to know each as an individual and will share her knowledge and understanding of the individual with other professional members of the staff. Social workers now functioning with our patients have become able to evaluate the information brought to them by the patients. They can distinguish between the ordinary "gripes" which arise out of a confining and isolated situation and the real problems which have a direct bearing on medical treatment and should be brought to the attention of the doctor in charge of the case. Social and financial problems of the patient she can take direct action upon with the agencies which can be of constructive help. This relieves the patient's mind which, in turn, helps to hasten recovery. We have no desire to "mollycoddle" our patients. Our aim is to help the patient to help himself. I can definitely state that the efforts of our social workers have helped to change the attitude and behavior of a good many of our patients.

Surgical and Diagnostic Problems

Cases are transferred to the Colorado General Hospital in Denver when, in the opinion of the conference, surgery is advisable or if some complicating condition needing special study is present. Two of our institutions are wings of general hospitals, well-equipped to carry out most diagnostic procedures including planigrams but not complete pulmonary function studies. Therefore, most of our cases for chest surgery go to the Colorado General Hospital for final evaluation. This Hospital is affiliated with the University of Colorado School of Medicine. Here pulmonary function studies are done. In 1947 the legislature appropriated funds for a special ward, exclusively for the use of tuberculosis cases, chiefly those on the state program. This is the only state-owned facility we have and it has a total of 26 beds. All chest surgery is performed at this institution with the exception of emergencies and a few chest cases when the ward is full and it seems inadvisable and uneconomic to postpone surgery. Also, almost all fusions for tuberculosis of the bones and joints are done at Glockner-Penrose Hospital in Colorado Springs where we have had access to unusual facilities and surgical interest and skill in this very specialized field which did not seem to be available elsewhere.

Upon completion of surgery and the immediate postoperative period the patient is transferred back to the sanatorium from where he came, for from six to nine months of bedrest, drug therapy and final ambulation before discharge.

Ambulant Centers

We have one institution where ambulant care only is provided—Sunnyrest Sanatorium in Colorado Springs. Patients are transferred here from the other facilities in Colorado Springs and La Junta and sometimes Denver for final ambulation—usually a three or four months' process. These cases are sputum negative and are undergoing a prescribed exercise schedule. A cooking school and facilities for learning to type are available at Sunnyrest; also, a bookkeeping course is given. A somewhat similar facility is open to us in Denver at Craig Colony for male patients only. Sunnyrest is a valuable adjunct to our program. Our patients really get a physical workout there and are usually able to resume their former occupation soon after their discharge. Also, it has been valuable to place patients here who have lost their drive or ambition to "get going" after prolonged hospital care. When they are placed in this group of ambulant patients, most of whom are anxious to get back into the work-a-day-world, these cautious or neurotic individuals soon become imbued with the same spirit of once more resuming their place in the world. We have an outpatient department to which cases of pneumoperitoneum in the institutions can be discharged in order to continue this treatment and drug therapy. If the patient lives in or near the city in which he is hospitalized he continues under the care of the same physican. All services and procedures are paid for at the same rates that prevail in the institution. Refills are done at the physician's office or at the sanatorium. If the patient lives at a distance he receives his refills from a physician skilled in this procedure who also has experience in tuberculosis and lives nearest the patient's home. If there are several in the locality, the patient is given his choice.

Recently we have embarked, in cooperation with Dr. Hilbert Mark, Director of Tuberculosis Control, Denver, on a pilot study of home care covering a small group of patients living in Denver who fall into one of several categories.

(1) Maximum benefit from prolonged hospitalization with sputum still positive.

(2) Cases that cannot successfully be handled in the sanatorium for disciplinary reasons.

(3) Elderly persons with positive sputum but having a sluggish type of disease who it is believed will have difficulty in adjusting to life away from home.

In every instance the home situation is cleared with the Public Health Department and the agreement of the patient to continue supervision of his home by the Public Health Nurse is secured. The case is also cleared as to medical indigency by the Welfare Department. Treatment is under supervision of the Denver Tuberculosis Clinic and an all-inclusive rate of $30 a month is paid from State and County funds through the Division of Tuberculosis Hospitalization. It is my opinion that every individual with tuberculosis is benefited by a few months, at least, in a sanatorium

where he is taught something about the disease and how to protect himself and others.

What Are The Costs?

The present annual cost of operating the Division of Tuberculosis Hospitalization is approximately $600,000, of which amount the County Welfare Departments contribute approximately half. About 500 patients were given care last year. Our daily average case load is now approximately 250 under hospitalization and 40 to 50 out-patients or on home care in Denver. The total per day cost last month was $7.48 per patient. (True costs would probably run about $8.50 per day, since all services are not now paid, as is explained later.) Per day costs for tuberculosis care in states which appear to be giving comparable care in state institutions recently visited by me seem to run 20 to 30 per cent higher than do our costs. This is not surprising since most privately run institutions always seem to be somewhat more efficiently operated.

What Are The Results?

For the first 11 months of 1953 our discharges have been as follows:

	per cent
*discharged as inactive or arrested	57
*discharged on home care	0.5
discharged as active (NTA 1950 classification)**	5
discharged as dead	9
discharged as leaving against medical advice	18
*discharged to the out-patient department with disease arrested	10.5
discharged as non-tuberculous	0.5
disciplinary discharges	0.5

*Together total 68 per cent, or over two thirds total cases terminated.
**Chiefly cases with negative sputum but with x-ray evidence (possibly only on tomograms) of cavity.

These figures will compare favorably with those of state sanatoria where good care is provided. It must be remembered that last year (latest figures available) our new admissions were 66 per cent in the far-advanced class, 21 per cent in the moderately advanced category and 13 per cent minimal in extent. Last year only 4 per cent of admissions represented cases discharged from our program in the two previous years as inactive or arrested. It must be remembered that these are all welfare cases and go back, in many instances, to inadequate homes and inadequate nutrition. Therefore, this relapse rate does not seem unduly high.

What Are The Disadvantages Of Colorado's Unique System Of Care?

(1) We have more difficulty in achieving a smooth continuity and transfer of information when patients are transferred from the sanatoria to the Colorado General Hospital for surgery than if all our patients were under one roof.

(2) Due to transfers of some patients from hospitals or sanatoria to

ambulant centers or public health clinics in the larger cities following discharge, plans for rehabilitation sometimes get confused or delayed.

(3) There is some variation between the efficiency of the County Welfare Departments in processing cases and a difference in the standards set up for medical indigency. I would state here that only two or three of our County Welfare Departments among the 63 in the state are not now employing a liberal interpretation of medical indigency.

(4) Considerable time is spent by the director and his staff in travel between institutions. These institutions are scattered over an area of about 200 miles. This time which costs money and energy would not be consumed if all patients were under one roof.

(5) The records of patients are not quite as readily available or, in some instances, as adequate as those usually found in a good State institution.

(6) The Colorado plan is not popular with the National Tuberculosis Association and (to a lesser degree) with the Colorado State Tuberculosis Association. It sounds more complicated than it is in actual operation. Some think it wrong to be different. I believe, we are the only state without a state sanatorium or a system of county institutions for the care of the needy tuberculous.

(7) The director has a difficult public relations job dealing with 11 different institutions. He has to make many important decisions singlehanded every day and has almost unlimited power as to policy. It is true that he is responsible to the Colorado State Board of Public Welfare but there is only one physician on the board and he is able to give only limited time to the problems of this division. If the director plays politics or favorites great harm can be done since much depends upon a condition of mutual confidence between the patients and the institutions and our division. The director alone approves all the bills on all the patients though there is a check at the county level when copies reach the auditing offices of the local Welfare Departments. If there is a conflict between the vital needs of the patients and the outcries of the taxpayers we usually try to resolve the problem in favor of the patients.

(8) If and when Colorado passes a compulsory hospitalization law to take the most recalcitrant persons with positive sputum out of circulation there is no institution with locked doors and barred windows in which to place him. Quite possibly none of the sanatoria we now use would be interested in furnishing such accommodations. Also, there are a few cases each year such as alcoholics, psychotics and behavior problems that cannot be handled with our present setup. There is a good tuberculosis ward at the State Hospital for the Insane at Pueblo for the psychotic or alcoholic patient but commitment must be arranged. Commitment laws are archaic in Colorado and County Health or Welfare Departments are loathe to press for commitment. This is a valid criticism and involves two to four patients each year. They usually come from Denver and have to be taken care of by that city in their own tuberculosis ward at the Denver General Hospital.

Advantages Of The Plan

(1) Patients can be hospitalized near home.

(2) Existing facilities are utilized. It is advantageous to the institutions to have us fill their empty beds. Our state program has had no waiting list for four years.

(3) The institutions are smaller for the most part than would be a state sanatorium—more homelike and they are able to serve more tasteful food.

(4) Over half of the institutions have a religious background. This seems to lead to fewer disciplinary problems and greater peace of mind among patients hospitalized in them, especially if they are of their own faith.

(5) If the patient does not adjust well to one institution, he can be tried in another. Almost always a proper adjustment can finally be made.

(6) Disciplinary problems can be moved farther and farther from home but at the same time kept under care.

(7) The patients like being the responsibility of one physician for their day-to-day care. Most of the physicians in charge of our cases are men with years of experience in tuberculosis. Most patients do not seem to like changes in physicians.

(8) Our patients like being hospitalized with private patients. This boosts their morale. No discrimination is permitted in the sanatoria between private and state patients, or is there segregation of race or color. This was a hard nut to crack, but it has been at last successfully cracked except possibly in the case of one institution.

(9) We have been successful in raising standards of medical and nursing care in some institutions where this has been necessary. This benefits private patients as well as our state cases.

(10) Costs of care appear to be less by 20 to 30 per cent than costs in states giving comparable care in state or county-run institutions.

(11) Our rate of discharges against medical advice (about 18 per cent of total discharges including deaths) is considerably below the national average—an indication that patients like their care.

(12) I have found that the top flight physicians and surgeons of the state are willing to serve our patients on a part-time basis at reasonable fees and, in some instances, at no fee at all. Chest surgeons contribute their operative services as part of their teaching at the medical school. They are paid for services at all conferences, however, though this represents only a small total remuneration.

(13) Our system of care is as far removed from state medicine as it is possible to place it, using, as we do, existing facilities and part-time private physicians. I am the only full-time medical man on the program. It is realized that the care of tuberculosis has come to be recognized for the majority of patients as one that must be socialized because of the economic and public health problems involved.

In the past seven years the death rate from all forms of tuberculosis

in my state has dropped much more rapidly than for the country as a whole. In 1945, according to National Tuberculosis Association statistics, there were 26 states in this country that had lower death rates from tuberculosis than did Colorado. In 1952 we had improved to the point where only 15 states had a lower death rate from this disease than did Colorado. I do not, for a minute, wish to imply that our Division was entirely responsible for this marked improvement. It has been the result of cooperative effort on the part of all state and private agencies interested in the control of tuberculosis.

SUMMARY

Colorado has been successful in treating state cases of tuberculosis in private sanatoria or wards of general hospitals, including isolation wards, set aside for this purpose, instead of maintaining state facilities. The type of care is under close supervision with frequent conferences between the state Division of Tuberculosis Hospitalization and the staffs of the institutions. The costs of care are somewhat less than might be expected if the state maintained its own facilities. Cases are transferred for surgery to a central institution which is connected with the Colorado School of Medicine.

The advantages and disadvantages of the program are enumerated. The advantages seem to considerably outweigh the disadvantages. The results compare favorably with those obtained from the use of state sanatoria.

RESUMEN

El Estado de Colorado ha tenido éxito tratando los casos del Estado, de tuberculosis alojándolos en sanatorios privados, salas de hospitales generales, incluso en las salas de aislamiento adecuadas para ese fin en lugar de mantener servicios del Estado. La forma de tratamiento es estrechadamente vigilada habiendo frecuentes conferencias entre el Departamento de Hospitalización de Tuberculosos y el personal de las instituciones.

Los costos son algo más bajos de lo que podría esperarse si el Estado mantuviese sus propios establecimientos. Los casos son enviados para los servicios de cirugía cuando lo requieren, a una institución central que está en relación con la Escuela de Medicina de Colorado.

Se enumeran las ventajas y las desventajas de este proceder.

Las ventajas parecen sobrepasar considerablemente a las desventajas. Los resultados pueden compararse favorablemente con los obtenidos en los sanatorios del Estado.

Malignant Mediastinal Teratoma Simulating Cardiovascular Disease

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Several writers[1,2,3] have reviewed the subject of mediastinal tumors and have concluded that they are rare. Blades[4] stated that "mediastinal tumors though rare are probably much more common than was previously believed to be the case." He collected 109 cases[5] which had come to operation in five Army thoracic centers. Of these, six were malignant teratomas. The teratomas are a small group of tumors which usually take their origin in the anterior mediastinum. From the total cases of mediastinal dermoids and teratomas collected until 1945, there were only 42 authenticated cases of trigerminal teratomas. According to Rusby[6] 11.9 per cent of teratomas of the mediastinum are malignant. In the archives of this general hospital having an average census of approximately 1500 patients, over a period of 10 years there are records of only two with a diagnosis of malignant mediastinal teratoma. Careful investigation of one of these records leads one to doubt the accuracy of the diagnosis, which was not confirmed definitely by the pathologist after operation, and no autopsy was performed after the patient's demise.

Case Report

A 23 year old white male, was admitted to this hospital on September 4, 1952, with complaints of increasing fatigability and precordial pain radiating into the left shoulder, left side of the neck and down the ulnar surface of the left arm, which began in March 1952. The onset of the pain was mild, but gradually increased, especially upon effort.

Past history revealed normal chest findings upon enlistment in the U. S. Navy during May 1951. A photofluorogram (70 mm.) of the chest taken during December 1951 was reported normal. An x-ray film of the chest on July 7, 1952 revealed the presence of an abnormal cardiac shadow; lateral view failed to yield any additional information. On September 4, 1952, a systolic murmur was heard over the heart and he was admitted to the hospital. Upon entry it was described as a harsh, low-pitched, pulmonic systolic murmur, with a palpable thrill, and a diagnosis of rheumatic valvular disease was considered. The erythrocyte sedimentation rate was 22 mm./hr. and 30 mm./hr. An angiocardiogram on September 17, 1952 was inconclusive. On September 30, 1952, anginal pain developed and was not relieved by nitroglycerin. On October 13, 1952, cardiac fluoroscopy indicated a mass in the mediastinum, probably due to lymph nodes. Repeated electrocardiograms were within normal limits. On October 16, 1952, a right, retroclavicular fat pad biopsy was reported as normal tissue. On October 22, 1952, he was presented to the Thoracic Disease Conference where the following recommendations were made: 1) liver function studies, 2) intravenous pyelography, and 3) thoracotomy. At this time he had lost 15 pounds since his hospitalization. Liver function tests and intravenous pyelography were reported to be within normal limits.

Left thoracotomy was performed on October 29, 1952 and an anterior mediastinal tumor was found, involving the upper half of the pericardium and surrounding the phrenic nerve. The tumor was attached to the remnant of the thymus and to the left innominate vein. The dissection of the tumor from this latter structure was

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The opinions or assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

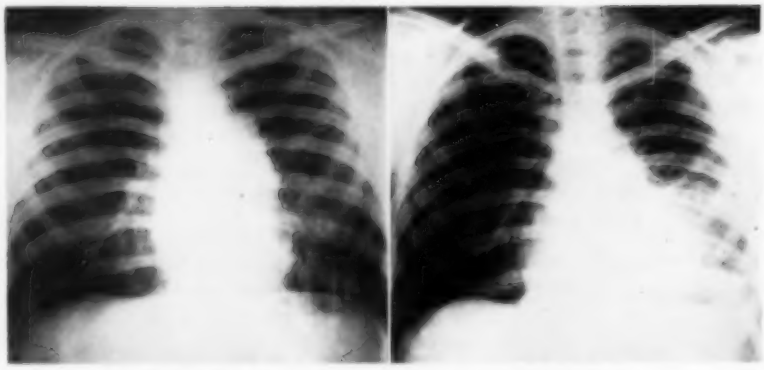

FIGURE 1 FIGURE 2

Figure 1: Chest film, preoperative, showing malignant teratoma in vicinity of pulmonary conus.—*Figure 2:* Chest film, postoperative, showing normal cardiac contour.

effected with some difficulty. After removing the tumor, including about 10 cm. of the phrenic nerve and most of the left half of the pericardium, the thrill which had been palpable in the pulmonary artery upon entry and at the beginning of operation was no longer present. Figure 2 represents the postoperative roentgenogram of the chest, showing the absence of the tumor shadow which had appeared in the preoperative x-ray film.

The microscopic pathologic report identified the specimen as malignant teratoma of trigerminal origin (Figures 3 and 4).

The immediate postoperative period was marked by absence of the preoperative symptoms and the precordial murmur. One and one-half months later he began to complain of a recurrence of substernal pain, and at this time a loud, harsh, systolic murmur was heard again over the pulmonic valve area. Nodules were observed in the healed incision and above it. Biopsy of one of these on December 14, 1952 revealed metastatic teratoma (Figure 5). His course became progressively worse and he expired on January 14, 1953.

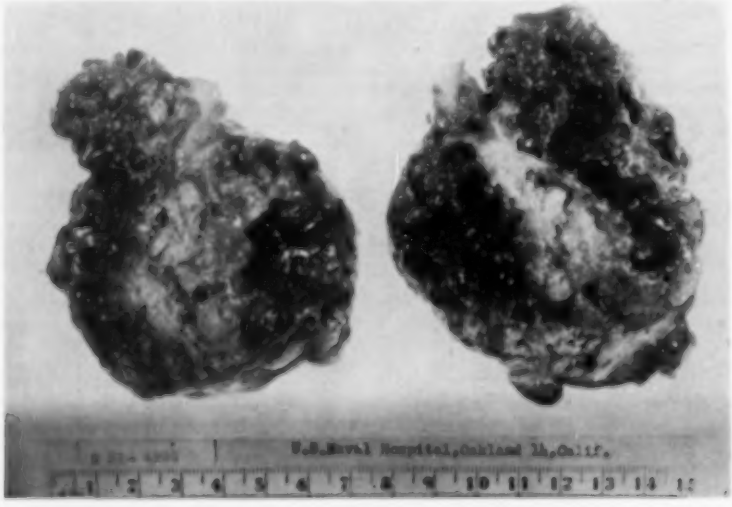

FIGURE 3: Photograph of gross specimen of mediastinal teratoma.

Postmortem examination revealed recurrence of the tumor in the mediastinum with infiltration about the base of the heart and great vessels (Figures 6A and B).

Discussion

This case of malignant trigerminal teratoma has been presented not so much because of its rarity as because of the clinical characteristics which caused it to be mistaken for heart disease. Mediastinal teratomas not infrequently masquerade as cardiac lesions; in fact, the differential diag-

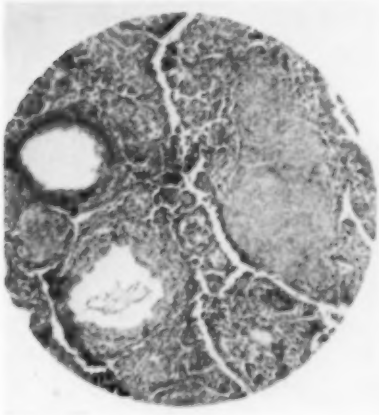

FIGURE 4

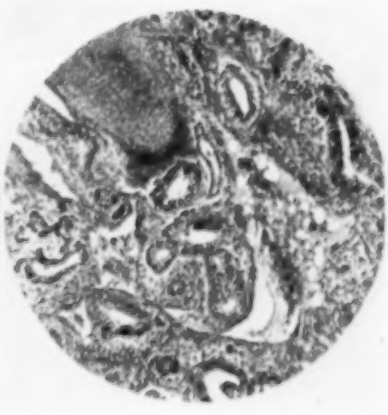

FIGURE 5

Figure 4: Photomicrograph, showing elements of three germ layers in malignant teratoma. (× 200).—*Figure 5:* Photomicrograph of metastasis, showing structure similar to Figure 4. (× 200).

FIGURE 6A

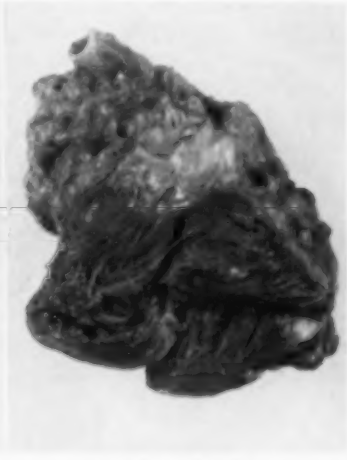

FIGURE 6B

Figure 6: Photograph of heart showing infiltration of recurrent tumor about base of heart and great vessels. *A*, left ventricular view; *B*, right ventricular view.

nosis of anterior mediastinal tumors is frequently difficult and errors in interpretation of physical signs and x-ray shadows are often made in this part of the body.

Such errors sometimes result in delay in operation as in the case reported by Skinner, Isbell, and Carr[7] and in the case reported here. Delay may be the factor responsible for death in some cases of malignant disease; hence, an awareness of possible errors in evaluating physical signs and x-ray shadows in the mediastinum should be ever present. In this case, there was an original error in diagnosis because of the mediastinal shadow seen on the roentgenogram (Figure 1), precordial pain, and a harsh, grade III, systolic murmur along the left side of the sternum with maximal intensity at the second rib. The murmur, as established at operation, was due to pressure of the tumor on the pulmonary artery, and it disappeared after removal of the growth. Murmur produced by the pressure of a mediastinal tumor, as in this case, is not often encountered and therefore easily leads to error of interpretation. Brewer and Dolley,[8] 1949, and Rusby,[6] 1944, reviewed the signs and symptoms produced by mediastinal teratomas and made special mention of the cardiac effects of the tumor, but murmur was not included in the physical signs recognized by these authors. Maier[9] described a case of teratoma attached to the pericardium in which there was a "harsh systolic murmur over the entire precordium." No mention was made whether the murmur disappeared after operation. The case reported here is the only one of record, found by the authors, in which a cardiovascular murmur was noted.

In the evaluation of cases of this nature the electrocardiogram may be of great benefit. Ackerman[10] suggested the use of cardiac catheterization in differential diagnosis of tumors of the mediastinum and heart lesions. Angiocardiography and tomography also may be very helpful. Pneumothorax has been used to separate tumor shadow from heart shadow. Fluoroscopy is of great value and in this case was the first indication that the tumor mass was separate from the heart. When the diagnostic data are all assembled and the diagnosis is still not certain, it is our conviction that open thoracotomy should be employed early. The only hope in treating teratoma is to remove the lesion while it is still benign. The present investigation has revealed no case of malignant mediastinal teratoma that has survived for five years. Our patient lived about 11 months after the onset of his symptoms. Case No. 34202 of the Massachusetts General Hospital Case Records[11] was that of a young man discharged from the Army in good health one and one-half years before onset of illness, three months after which he died from malignant teratoma. His symptoms had been poorly localized shifting pain in the right side of the chest and weight loss of 15 pounds.

SUMMARY

A case of malignant trigerminal mediastinal teratoma has been presented, with a brief summary of reviews of mediastinal tumors made by other authors. Surgical removal of these tumors has been advocated by several authors.[5,6,12,13] With this we agree, but also wish to emphasize the

need for early operation following minimal delay in diagnostic procedures. The disease mortality is in the neighborhood of 100 per cent. The only hope for survival in the victim of teratoma of the mediastinum is extirpation of the tumor while it is still benign or before it has metastasized, or become irresectable.

RESUMEN

Se ha presentado un caso de teratoma maligno mediastinal trigémino con un resumen de revistas de tumores del mediastino hechos por otros autores. Se ha aconsejado por varios autores, la extirpación quirúrgica (5, 6, 12, 13). Estamos de acuerdo en esto, pero también deseamos recalcar la necesidad de una operación temprana después del diagnosis. La mortalidad de la enfermedad está en las cercanías del 100 por ciento. La única esperanza para la sobrevida de la víctima de teratoma del mediastino es la extirpación del tumor mientras que sea aún benigno o antes de que sehaya metastatizado o sea irresecable.

RESUME

L'auteur présente un cas de tératome trigerminal du médiastin, ainsi qu'un court résumé de la littérature concernant les tumeurs médiastinales. L'extirpation chirurgicale de ces tumeurs a été préconisée par plusieurs auteurs. Lui-même y donne son accord, mais il tient à mettre l'accent sur la nécessité d'une opération précoce dans les délais les plus rapides après que le diagnostic aura été fait. La mortalité de cette affection est proche de 100%. Le seul espoir de survie du malade atteint de tératome du médiastin est l'exérèse de la tumeur pendant qu'elle est encore bénigne, ou avant qu'elle n'ait produit des métastases ou soit devenue inopérable

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The Electrocardiographic Pattern in Venous Air Embolism

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Air embolism is one of the most fearful and fatal complications of pneumotherapy in tuberculosis.[1] Air entering the circulation in the course of artificial pneumothorax, generally proceeds by way of the pulmonary veins to the left side of the heart and thence to the systemic circulation, producing the characteristic symptomatology of organ ischemia or infarction especially myocardial or cerebral. Air entering veins other than the pulmonary veins, as in the course of artificial pneumoperitoneum, affects primarily the right side of the heart. Amounts of over 100 cc. of air in the right side of the heart cause obstruction to blood flow and dilatation with resultant ischemia of its musculature. Even smaller amounts may cause fibrin clots or thrombosis and obstruct cardiac blood flow.

These effects are reflected by the electrocardiogram as ST-T segment changes, arrhythmias, various degrees of A-V block and intraventricular conduction delay or bundle branch block. Although the diagnosis of air embolism is often obvious because of its dramatic symptoms, sometimes the clinical picture may be vague and misleading, especially when smaller amounts of air enter the circulation and the vital organs are little or not affected. The electrocardiogram in this instance may be helpful in differentiating air embolism from other complications and thus affords a valuable laboratory aid in diagnosis.

Most of the reported cases of air embolism have died so soon after the injection of air, that there has been no time to study the patient or to obtain electrocardiograms. Groedel[2] reported that, in a woman who died 24 hours after peri-renal insufflation of air, an electrocardiogram taken before death showed complete A-V block with changes suggesting myocardial ischemia. Durant[3] has reported that when air is injected experimentally, into the femoral veins of dogs, sharp inversion of the T wave takes place (first-stage ischemia), then ST segment deviations occur (second-stage ischemia, injury phase) and finally marked alterations of the QRS complexes indicate conduction changes which may terminate finally in intra-ventricular block and ventricular fibrillation.

Over 100 instances of air embolism following pneumoperitoneum have been reported in the literature, including nine cases at Olive View Sanatorium.[4] Three cases of right-sided air embolisms with electrocardiographic tracings which illustrate right-heart involvement are presented here. Two of these patients survived the air embolism and the electrocardiogram returned to normal, while one who showed a right bundle branch block died with a mural thrombus following the air embolism,

as shown at autopsy.

Katz[5] has called attention to a characteristic electrocardiographic pattern which he ascribes to heart strain, although there is still some dispute as to its exact significance. An inverted QRS or deep S wave in lead I, with an upright QRS in lead III, together with a depressed or inverted ST-T pattern in lead III and in the chest leads over the right side of the heart are usually attributed to right heart strain. P-pulmonale, indicated by a small P_1 with peaked P_{2-3} and sometimes inverted P in the chest leads further points to right heart involvement.

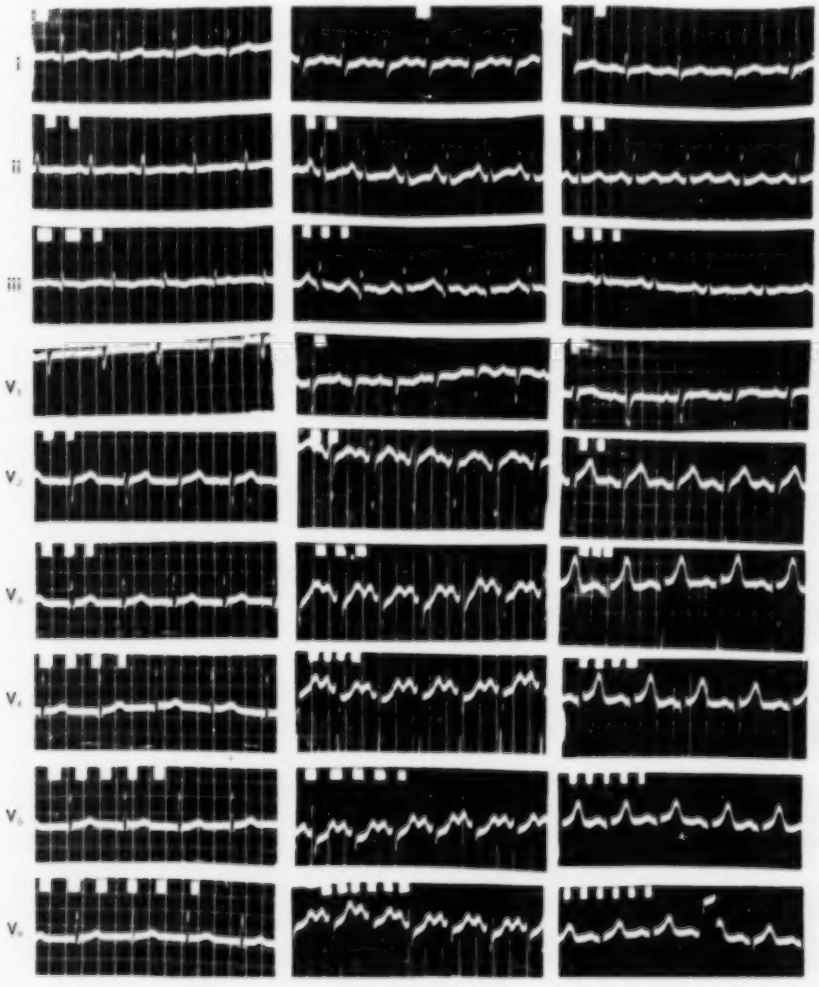

FIGURE 1A FIGURE 1B FIGURE 1C

Figure 1A: Normal electrocardiogram. *Figure 1B:* Immediately after embolism.—*Figure 1C:* Electrocardiogram returning to normal six months later.

Figure 1 shows a normal electrocardiogram taken months prior to the patient's air embolism. A few hours following the acute episode of air embolism, an electrocardiogram (Fig. 1B) showed an increased cardiac rate, the appearance of a deep Sl, small Q_3, elevated $T_{V_{2-6}}$ and peaked $P_{2,3}$, V_{1-6}. A later electrocardiogram taken six months later shows a return to a more normal pattern but still with a high $T_{V_{2-6}}$.

In Fig. 2 no previous electrocardiograms were available and a tracing taken a few hours after this patient's air embolism, shows a rapid

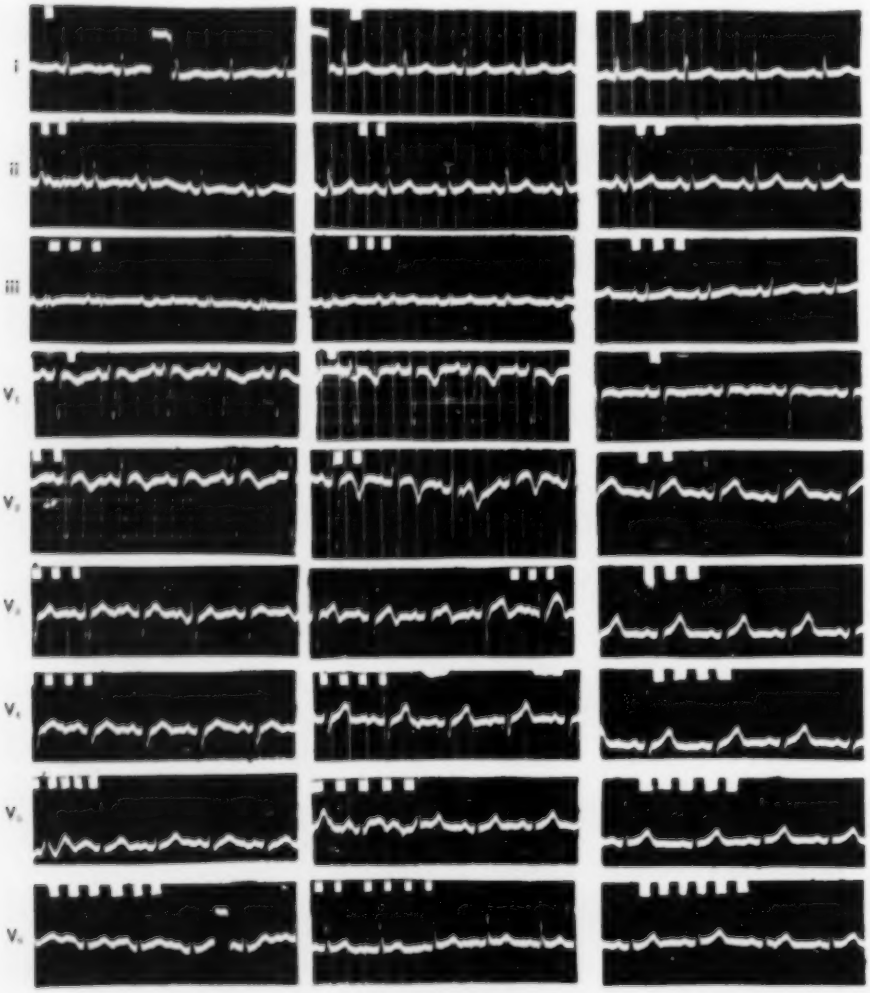

FIGURE 2A FIGURE 2B FIGURE 2C

Figure 2A: Electrocardiogram immediately after air embolism.—*Figure 2B:* Twelve days later.—*Figure 2C:* Twenty-six days later electrocardiogram returning to normal.

heart rate. In Fig. 2A the early changes of inversion of ST-T pattern in $V_{1,2}$ were noted. Twelve days later these T wave inversions extended to $V_{1,2,3}$. Finally 26 days later, the electrocardiogram returned to a normal pattern completing the cycle of right heart strain.

In Fig. 3 an electrocardiogram was not taken until the day before death and shows a typical interventricular block of the concordant inverted type. The QRS interval is 0.12 seconds and is inverted in all limb leads. Autopsy performed the following day disclosed a large mural thrombus almost completely filling the right auricle and acting as a ball valve obstruction to cardiac blood flow.

The above three examples give clinical support to Durant's experiments in dogs and illustrate how the electrocardiogram may aid in the diagnosis of right sided air embolism.

Durant has also shown experimentally that placing the animal on its left side relieves the intra-cardiac obstruction of pulmonary air embolism,

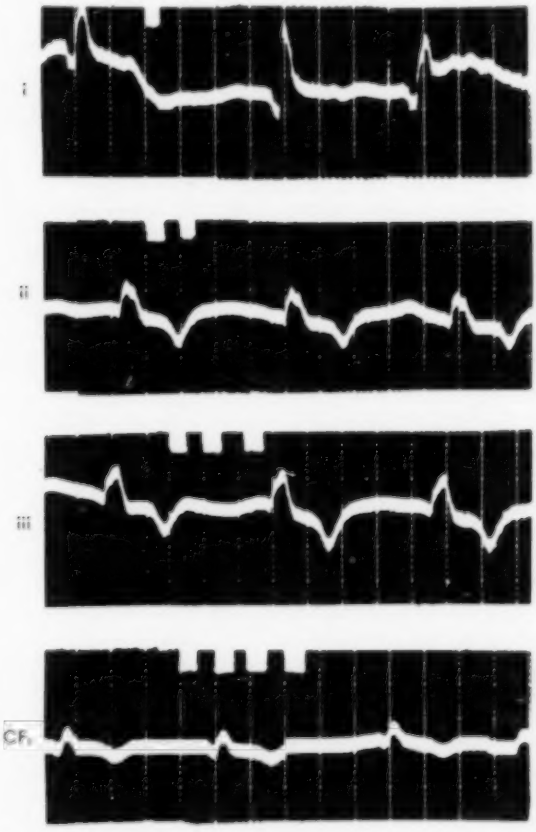

FIGURE 3: Bundle Branch Block with mural thrombus and air embolism, proved by autopsy.

as the air trapped in the right ventricular outflow tract floats toward the apex of the right ventricle and the electrocardiogram returns to normal. The air in the right ventricle is then churned into small bubbles and passes to the pulmonary vessels to be excreted by the lungs. Placing the patient in the left lateral position with the head down may be even more effective since air is then shunted away from the head and into the lower portions of the body, thus avoiding a fatal cerebral air embolism.

If an electrocardiogram is taken early and the diagnosis of an air embolism is established, the patient may be properly positioned and treated and thus be saved from serious complications or death.

SUMMARY

Three cases of right sided air embolism with electrocardiographic tracings demonstrate characteristic electrocardiographic patterns of right heart strain due to air embolism. Because of the diagnostic value of the specific electrocardiographic pattern of right heart strain, the electrocardiograph should be used early and often as an aid in the recognition of air embolism.

RESUMEN

Mediante los trazos electrocardiográficos en tres casos de embolia gaseosa del lado derecho, se demostraron aspectos característicos de esfuerzo del corazón derecho debidos a esa embolia.

A causa del valor diagnóstico del aspecto electrocardiográfico específico, ese trazo debe usarse de inmediato y a menudo para el descubrimiento de la embolia gaseosa.

RESUME

Les tracés électrocardiographiques ont démontré dans trois cas d'embolie gazeuse du côté droit des images caractéristiques d'atteinte du coeur droit. Etant donné la valeur diagnostique des tracés électrocardiographiques caractéristiques de l'atteinte du coeur droit, l'électrocardiographie devrait être utilisée précocément et souvent, pour permettre de reconnaitre l'embolie gazeuse.

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Diagnosis of Intrathoracic Meningocele*

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Intrathoracic meningocele is looked upon by many as a rare tumor of the thoracic cavity. Its diagnosis is usually not made preoperatively. Among the twenty-odd certain cases reported in the literature there are no more than 4 diagnosed with certainty without thoracotomy (Schüller and Uiberall 1938, Head 1949, Cross and co-workers 1949, Cmyral 1952, and Scars, Clayton and Siebel 1953); to these is to be added the case now reported. Intrathoracic meningocele is very often accompanied by von Recklinghausen's cutaneous neurofibromatosis and characteristic skeletal changes. If, in addition, radiographic examination reveals an intrathoracic tumor, there is every reason to suspect the presence of a meningocele. On the other hand, when there is reason for such suspicion, it is not too difficult to find out, by means of myelography or puncture, whether the cyst communicates with the subarachnoid space or not. The diagnostic difficulties are mainly due to the fact that intrathoracic meningocele is seldom encountered even in large hospitals and doctors consequently have little experience with it.

In the past two years, two cases of intrathoracic meningocele have been treated at First Surgical University Clinic, Helsinki. In one of these cases, published previously by one of us (M.T. 1952), the diagnosis was not established until operation. In the other case, the diagnosis was confirmed preoperatively by air myelography. Since this case exhibited all the typical features of intrathoracic meningocele, the following report of it will be found justified.

CASE REPORT

A man aged 56 years, admitted to the clinic on Feb. 2, 1953. As long back as he could remember he had had reddish nodules and brownish patches on his skin. After the age of 20, he became aware of increasing spinal deformity. For the past 10 years he had suffered from breathlessness and cough, particularly on effort and in cold weather. The dyspnea had aggravated lately, and the patient had been hardly capable of work. There had also been back pain between the shoulder blades on exertion. Eight years before admission x-ray examination of the chest had revealed an intrathoracic tumor, interpreted as of benign character.

Physical Examination.—The patient was small and slender, in a fair general condition. The skin of the trunk, head, arms, and thighs showed reddish nodules ranging in size from a pin-head to a cherry, and cafe-au-lait patches. The neck was short and the cervical spine greatly deformed. The thoracic spine was also deformed, with kyphoscoliosis about the middle (Fig. 1). The lungs were markedly emphysematous, but otherwise thoracic and abdominal examination revealed nothing pathologic. Neurologic examination also yielded a negative result. The blood sedimentation rate was 14 mm. in an hour. All the other routine laboratory examinations gave a normal result.

X-ray Examination of the Chest.—The seventh and eighth thoracic vertebrae were wedged, giving rise to an acute kyphosis with the apex at the seventh vertebra and to slight scoliosis convex to the left at the same level. There was well-marked scalloping on the posterior and left lateral aspects of the sixth to ninth vertebral bodies, but the intervening disc spaces were unaffected (Fig. 3 *b*). The left pedicles of the

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seventh and eighth vertebrae were completely destroyed (Fig. 3 *a*), the spinous processes of these vertebrae turning backwards (Fig. 3 *b*) and to the right (Fig. 3 *a*). The left intervertebral foramina of these vertebrae formed one large opening (Fig. 3 *b*). The seventh intercostal space was increased in width at its dorsal ends, and the related ribs were eroded. The seventh rib showed an upward subluxation at its vertebral end (Fig. 2 *b*). A rounded, well-circumscribed, homogenous tumor, measuring 10 by 8 cm, was seen in the posterior mediastinum left of the spine, at the level of the sixth to the ninth thoracic vertebrae (Fig. 2 *a*). The lungs were emphysematous, but otherwise the chest showed nothing abnormal.

Since the presence of von Recklinghausen's disease and of skeletal changes of the chest suggested that the tumor in the posterior mediastinum was a meningocele, air myelography was carried out. Sixty cubic centimeters of cerebrospinal fluid were withdrawn by lumbar puncture and replaced by air. With the patient lying on his right side, and the upper part of the trunk lifted up, the air was seen to rise into the sac-like tumor of the thoracic cavity and to form a semilunar air bubble along its

FIGURE 1A

FIGURE 1B

FIGURE 2A

FIGURE 2B

upper contour (Fig. 4, *a* and *b*). The location of the air bubble varied according to the patient's posture (Fig. 4*c*). When he lay on his left side, the air was seen to return to the subarachnoid space. Later, the presence of air could be established in the enlarged ventricles of the brain.

Since the progressive troubles of the patient, particularly the back pain, were evidently due to the meningocele, excision of the tumor was carried out (Prof. P. E. A. Nylander). The approach was made through the bed of the resected fifth rib, and the thin-walled cyst the size of a tennis ball was detached from its surroundings. It communicated with the spinal canal through a pedicle the lumen of which was passable by a finger. The meningocele was excised, and the resultant dural opening was closed by dural and pleural flaps. A drain was placed into the pleural cavity, and the wound closed in the usual way. The patient's convalescence was uneventful.

Pathologic Report.—The tumor was a thin-walled sac with a smooth inner surface. Histologically, the wall consisted mainly of proliferative arachnoidea. Some thinned dura could also be seen, partly attached to the arachnoidea, partly separate.

Discussion

In this case of intrathoracic meningocele all the pathologic features were present which are generally taken to characterise this rare cystic tumor of the posterior mediastinum (cf. Pohl 1933, Mendelsohn and Kay 1949, Byron and co-workers 1949, Ciaglia 1952, Kessel 1952, Turunen 1952, Cmyral 1952). Among these, von Recklinghausen's neurofibromatosis of the skin was most striking. It seems to be almost regularly present in conjunction with intrathoracic meningocele, that in more than a half of the reported cases von Recklinghausen's disease has also been diagnosed. Reddish, often pedunculated nodules and cafe-au-lait patches on the skin and a radiographically detected rounded, well-circumscribed tumor constitute such a remarkable association that a suspicion of intrathoracic meningocele is fully justified.

Characteristic skeletal changes lend support to such a suspicion. In the case now reported and in most of those published previously, spinal deformity extended up to the neck (Fig. 1*b*). The most characteristic of these changes was thoracic kyphoscoliosis at the level of the tumor. The

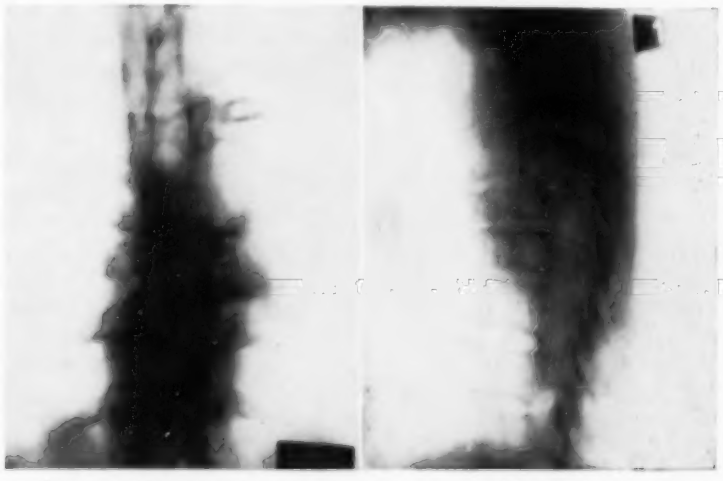

FIGURE 3A FIGURE 3B

FIGURE 4C

FIGURE 4B

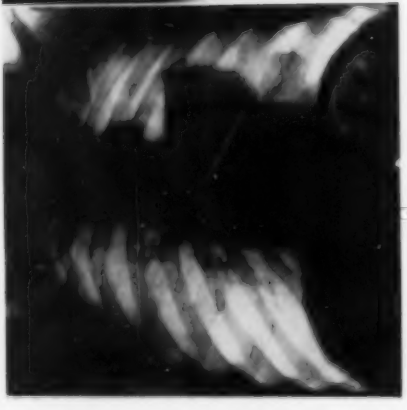

FIGURE 4A

semilunar erosions in the posterior and left lateral aspects of the vertebrae related to the meningocele were particularly interesting. Their shape (Fig. 3 *b*) resembled the scalloping caused by an aneurysm in the anterior vertebral aspects, and the assumption readily suggested itself that changes of pressure in the subarachnoid space involved the meningocele (e.g., Sengpiel and co-workers 1948) and eroded the bone of the vertebral surfaces without affecting the elastic intervertebral disc. Dolley (1949) has pointed out the similarity in the etiology of vertebral erosions caused by an aneurysm and those caused by a meningocele.

In the case here reported, the left side pedicles of the vertebrae adjoining the meningocele had become almost completely destroyed and the pedicles on the right side showed some erosion. On the left side, therefore, the intervertebral foramina formed one large opening. The spinous processes and the related neural arch turned backwards and towards the right. The spinal canal was greatly distended at this point, and a sagittal tomogram taken of this part of the thoracic spine (Fig. 3 *b*) had a great resemblance to the post-mortem preparation described by Ameulle and co-workers (1948) in which the spinal canal and dural sheath were extensively dilated in the vicinity of the meningocele.

Von Recklinghausen's neurofibromatosis, certain skeletal changes, and intrathoracic meningocele constitute such a well-established association that it seems most unlikely that they have no causal correlation with one another. There are writers, such as Sengpiel and co-workers (1948) and Ciaglia (1952), who believe that an intrathoracic meningocele is the result of congenital malformation, though most authorities seem to ascribe it to neurofibromatosis. Brook and Lehman (1924) showed that periosteal neurofibromas produce osseous changes of the type which Pohl (1933) thought to be responsible for the rise of a meningocele. Cross and co-workers (1949), on the other hand, think that a meningocele arises in a diseased dura and that the osseous changes only provide favorable circumstances for its appearance.

The case here reported seems to allow a few assumptions concerning the causal correlation between neurofibromatosis, skeletal changes, and intrathoracic meningocele. First of all, the patient reported having had the cutaneous lesions of neurofibromatosis since early childhood, but not having noted the progressive spinal deformity until his twenties. The intrathoracic tumor was not recognized until the patient was 48 years of age. This suggests that the primary disease was neurofibromatosis. The extensive erosions of the posterior vertebral surfaces and of the pedicles, which had produced a dilatation of the spinal canal (Fig. 3), suggested a disease of the dura which made it too weak to resist the pressure in the subarachnoid space. The protrusion of the sac-like dilatation of the intra-spinal meninges through the enlarged intervertebral foramen and widened intercostal space into the thoracic cavity seems to have been a later process. The case, thus, lends support to the view concerning the causative mechanism of intrathoracic meningocele advanced by Cross and co-workers.

The presence of von Recklinghausen's disease and of certain changes of the spine and ribs suggests but does not prove that an intrathoracic tumor discovered radiographically is a meningocele, for other cystic tumors and neurofibromas of the posterior mediastinum may be responsible for similar skeletal changes. The diagnosis of intrathoracic meningocele has, therefore, to be checked by finding out whether the tumor is a thin-walled cyst connected with the subarachnoid space. Schüller and Uiberall (1938) injected lipiodol into the spinal canal and noted that it found its way into the meningocele. Byron and co-workers (1949) and Cmyral (1952) injected some contrast medium into the meningocele, from which it flowed into the subarachnoid space. Head (1949) carried out simultaneous puncture of the tumor and of the lumbar spinal canal and found that the removal of part of the cerebrospinal fluid decreased the pressure in the tumor. Cross and co-workers (1949) used air myelography and found that air moved from the subarachnoid space into the tumor.

In the case reported in this paper the diagnosis of intrathoracic meningocele was also confirmed by air myelography. This proved to be an easy diagnostic method. The air passed easily into the meningocele, where its presence was easily recognizable in the radiograms. It was also possible to watch the passage of air from the meningocele into the subarachnoid space and back by altering the patient's posture. Air myelography seems to be a highly suitable method of confirming the diagnosis of intrathoracic meningocele. It is only when the lumen of the pedicle is obstructed that air myelography is of no use; the diagnosis has then to be confirmed by thoracotomy.

SUMMARY

The correlation between neurofibromatosis, certain skeletal changes, and intrathoracic meningocele is discussed and attention is called to the close association between these conditions. The significance of air myelography is pointed out and an interesting case reported.

RESUMEN

La correlación entre neurofibromatosis, ciertos cambios esqueléticos y el meningocele intratorácico se discute y se llama la atención sobre la estrecha relación existente entre estas condiciones patológicas. Se señala la significación de la mielografía con aire y se relata un caso.

RESUME

Les auteurs discutent la relation qui unit la neurofibromatose, certaines altérations du squelette, et le méningocèle intrathoracique. Ils attirent l'attention sur les rapports étroits qui associent ces différents éléments. Ils mettent en évidence la valeur de la myéographie gazeuse, et rapportent un cas intéressant.

Bibliography will appear in reprint.

Safer Pneumoperitoneum Refills

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Although much has been written relative to the role of pneumoperitoneum in the treatment of pulmonary tuberculosis, there still remain many unanswered questions pertaining to its therapeutic efficacy, the incidence of abdominal fluid formation, complications, the optimum position of the elevated leaves of the diaphragm, the duration of treatment, etc. Similarly, much has been written relative to the best site for inserting the needle into the abdominal wall or even the lower intercostal spaces. It is believed worth while to mention one aspect of technique which has rarely been presented.

As a rule, patients about to receive a pneumoperitoneum refill lie on the back with or without a pillow under the head. Some are tense, some are relaxed, others tend to push the abdominal wall towards the needle. Rarely does the operator pay any attention to the phase of respiration during which the needle is introduced into the abdominal cavity.

The illustrations shown graphically portray the differences in the height of the abdominal air space at the end of inspiration as compared with the end of expiration. The patients were advised to "take a deep breath, hold it, push." The needle was then quickly inserted through the abdominal wall.

It is well known that on inspiration the lungs expand, the diaphragm descends, and the contained abdominal air pushes the abdominal wall outward. It will be noted from the illustrations that the increase in height of the abdominal air space at the end of inspiration may reach approximately 40 to 50 per cent.

Marmion[1] reported a difference of 2 cm. between the height of the abdominal air space on deep inspiration as compared with normal inspiration. We have found that the difference is even greater when the extremes of deep inspiration and deep expiration are compared.

While the illustrations depict patients who had received air refills over a period of months, it is suggested that the difference in the height of the abdominal air space plays a more significant role as a safety technique factor in administering air refills to patients during the early course of pneumoperitoneum induction, and also when an unscheduled long period

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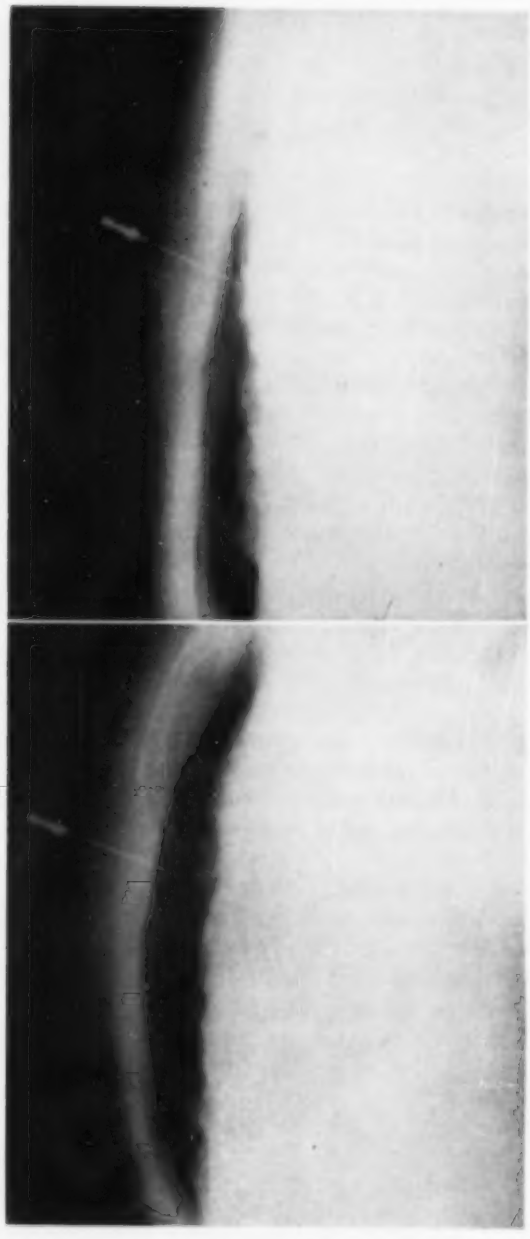

FIGURE 1A

FIGURE 1B

Figure 1A: First patient inspiration.—*Figure 1B*: First patient expiration.

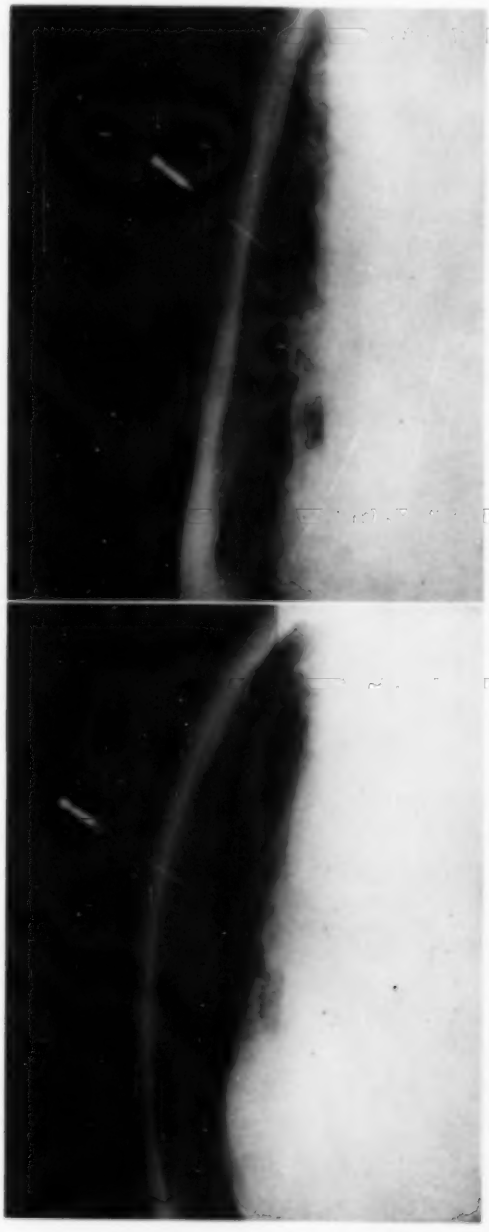

FIGURE 2A

FIGURE 2B

Figure 2A: Second patient inspiration.—*Figure 2B*: Second patient expiration.

FIGURE 3A

FIGURE 3B

Figure 3A: Third patient inspiration.—*Figure 3B:* Third patient expiration.

of time has elapsed between refills. By the use of this technique the danger of traumatising the underlying visceral contents should be minimized.

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SUMMARY

As shown in the illustrations, the height of the abdominal air space in a patient with artifically induced pneumoperitoneum is increased on deep inspiration as compared with expiration. It is therefore concluded that for those patients receiving pneumoperitoneum refills in whom an appreciable air space is not present, the insertion of the needle at the end of a deep inspiration is a safer procedure to reduce the danger of injuring the abdominal viscera.

RESUMEN

Como se ha mostrado en las ilustraciones la altura del aire en el neumoperitoneo artificial, aumenta en la inspiración profunda en comparación con la expiración. Se concluye por tanto para los enfermos que reciben neumoperitoneo en los que una capa de aire no es apreciable, la inserción de la aguja al final de una inspiración profunda es un procedimiento más seguro para reducir el peligro de lesionar las vísceras abdominales.

RESUME

Comme il est montré sur les planches, l'importance de la cavité aérique de l'abdomen chez un malade traité par pneumopéritoine est infiniment plus élevée dans l'inspiration profonde que dans l'expiration. Il en résulte que pour les malades à qui l'on insuffle un pneumopéitoine, lorsqu'il n'y a pas de cavité gazeuse suffisante, il est plus sûr de faire la piqûre à la fin d'une inspiration profonde, afin de réduire le danger be blesser les viscères abdominaux.

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the mental condition are based mainly on daily observations of the attending physician and the nursing personnel.

INH was given in doses ranging from 200 mg to 500 mg daily for periods from two weeks to one year. There was no selection on the basis of sex or race and the group ranged in age from 18 to 93 years. Various stages of pulmonary tuberculosis were present in 148, two had tuberculous lymphomas and two bone tuberculosis. The mental diagnoses were: schizophrenia 79, manic-depressive psychosis six, senility four, alcoholism eight, general paresis three, mental deficiency 12, cerebral arteriosclerosis nine, involutional psychosis two, Huntington's chorea one, sociopathic personality 25, mentally normal before INH medication and chest surgery were two and one was mentally normal before but had a history of hospitalization for manic-depressive psychosis eight years ago.

Our results in regard to tuberculous disease do not differ appreciably from the well-known results obtained by INH medication in any other tuberculosis hospital. These results have been described already in numerous articles.

There was apparently no connection between improvement of tuberculous disease and improvement or changes in the mental status.

Striking mental improvement could be observed in only one patient whereas 24 others showed mental improvement to a slighter degree. Patients, who had been uncooperative became cooperative. Hostile patients became friendly and sociable. Untidy ones became clean. Aggressive patients, who had formerly been in restraint for long periods, became quiet and could be taken out of restraint. Stuperous ones became more alert. These and similar changes could be observed.

On the other hand, two of our psychotic patients deteriorated in their mental condition during INH treatment and improved again promptly after discontinuation of the drug. In addition to those two we observed three who had been sent to us from another tuberculosis hospital, because they had developed acute psychosis during INH treatment.

None of the 25 patients, whose mental condition improved during INH treatment had received during the time of INH medication any kind of

TABLE I

Mental Diagnosis	No. of Pat.	Improved	Deterior.	No Change
Schizophrenia	79	13	1	65
Manic-depress. psych.	6	0	1	5
Involutional psychosis	2	0	0	2
Senility	4	1	0	3
Cerebral arterioscler.	9	2	0	7
General paresis	3	0	0	3
Huntington's chorea	1	0	0	1
Mental deficiency	12	2	0	10
Alcoholism	8	5	0	3
Sociopathic personality	25	2	0	23
Without psychosis before INH medication	3	0	3	0
	152	25	5	122

Mental Changes Observed in 152 Psychotic and Non-psychotic Patients During INH Medication

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Since Isonicotinic Acid Hydrazide (INH) treatment of pulmonary tuberculosis was started at the latter part of 1951, several reports have been published about unexpected side-effects of INH on the central nervous system and on the mental condition of mentally normal and psychotic patients. The first article in that regard was by Krieser and coworkers reporting about mental improvement of 44 per cent of 51 mentally ill tuberculosis patients during INH treatment[1]. Salzer and Lurie reported improvement of 68 per cent of their patients suffering from anxiety and depressive states by isoniazid treatment[3]. Other authors have observed the contrary, namely mental disturbances, apparently caused by INH medication. Vysniauskas and co-worker published recently an article describing five cases of severe reactions on the central nervous system following INH medication[2].

Observations similar to those described in the mentioned articles were made in the tuberculosis unit of the Oregon State Hospital, where we have used INH in the treatment of tuberculosis patients since May, 1952.

We have treated 152 patients by INH either alone or combined with Streptomycin, para-aminosalicylic acid, pneumoperitoneum, pneumothorax, phrenic crush or chest surgery of whom 149 have been mentally ill, mentally deficient, alcoholic or psychopaths prior to INH medication. Two had been mentally normal before INH medication and one was mentally normal during the last eight years prior to INH treatment but had been hospitalized for a manic-depression psychosis twice, eight and 10 years ago. Those three had been committed to the hospital because they developed acute psychosis during INH treatment, following extensive chest surgery in another tuberculosis hospital.

Prior to INH all patients were subjected to extensive laboratory studies including: chest x-ray films, complete blood count, sedimentation rate, blood sugar, blood urea nitrogen, urinalysis, kidney function and liver function tests and examination of the gastric contents on direct smear and culture for acidfast bacilli. All these procedures were repeated during and at the end of treatment.

Since we did not anticipate any effect of INH on the mental condition of our patients at the time we started our treatment program, no special psychological tests were given prior to INH. Only lately have we started psychological tests and electroencephalographic studies before starting them on INH. For this reason our experiences in regard to changes in

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shock treatment for their mental condition nor had they received shock treatment for at least several weeks before.

Case 1: A 50 year old white man was admitted to the hospital under court commitment in March 1950. Diagnosis on admission was schizophrenia, paranoid type. He was confused, disoriented, hallucinating and noisy. During the first months of hospitalization he was untidy, aggressive and violent and had to be kept in restraint. There was good improvement after electroshock treatment. He escaped in April 1952 and came back to the hospital two weeks later in the same poor condition as on admission in 1950. This time no improvement could be obtained by electroshock. He remained untidy, noisy and aggressive. In October 1952 he was started on INH for pulmonary tuberculosis. He received in the beginning 200 mg of INH daily and this dose was increased gradually to 500 mg daily. About one week after INH medication was started, he had an epileptiform seizure. There was no history of previous seizures and in spite of the increased dose of INH no other seizure occurred. From that time on he showed gradual improvement of his mental condition. After about three months of INH his personality and behavior had changed thoroughly. He now was quiet, cooperative, clean and friendly and had no hallucinations. Four months later, after having received INH treatment for seven months, he was paroled in considerably improved mental condition. No electroshock or any other treatment had been given to him for his mental illness during INH medication. We have not heard from him since.

Case 2: A 29 year old Chinese man was admitted to the tuberculosis unit on August 4, 1953. Three weeks prior he had undergone pulmonary resection and received since then 300 mg of INH daily. Soon after the operation he had become irrational, aggressive and expressed paranoid ideas. Therefore he was committed to our institution and INH treatment was discontinued. During the first two weeks of hospitalization his mental condition cleared up completely and remained so during his hospital stay and after his discharge on February 1, 1954 in spite of the fact INH medication was reinstituted in September 1953 and continued until February 1954 in a dose of 200 mg daily.

Case 3: A 27 year old white male was admitted on September 21, 1953 with a history of having been mentally normal until June 1953. At that time he underwent decortication of the left lung because of tuberculous empyema and was put on INH medication, 300 mg daily. Following this treatment he developed manic-depressive psychosis and was admitted here when INH was discontinued and replaced with streptomycin and PAS. His mental condition improved however only after he received a course of electroshock treatments. He was discharged on March 1954 in seemingly normal condition and has since been in good health.

Case 4: A 40 year old white woman was committed to the tuberculosis unit on January 29, 1954 with acute psychosis of a schizophrenic type. She had a history of having previously been a patient here because of mild manic-depressive psychosis, 10 and eight years ago, respectively. During the last eight years prior to this acute psychosis she had been in good mental health. On January 19, 1954 she underwent extensive chest surgery for pulmonary tuberculosis and was started on INH (200 mg daily). After the operation she developed severe acute psychosis. On admission she was completely disoriented and confused, untidy and aggressive and had to be spoonfed. For the first week of hospitalization here INH was continued and her mental and physical condition deteriorated. On the eighth day INH was replaced by streptomycin and PAS and from the same day on her mental condition improved rapidly. Within three days she appeared to be recovered and stayed so following her return to the tuberculosis hospital, from where she had come. Up to date she has remained in good mental health.

Discussion

It is a well known fact that INH, besides being a potent antituberculous drug, has a stimulating effect on the central nervous system. It can cause epileptic seizures of severe form in epileptics and its use is therefore inadvisable in such persons.[4] Besides this side-effect INH seems also to be able to influence the behavior and mental condition of psychotic and non-psychotic persons. Our experiences in this regard have been similar to those of other observers. We have seen that about 17 per cent of 149 mentally ill patients showed some kind of mental improvement during INH medication without having received any other psychiatric treatment during that time. On the other hand two of those 149 deteriorated mentally

during INH medication and improved again after discontinuation of the drug. Three, who had been in good mental health before INH medication became psychotic during a course of INH but recovered completely after discontinuance of the drug. One of these three patients had a history of a mild psychosis, eight years ago and another showed no recurrence of psychosis in spite of reinstitution of INH medication later on. Since these three patients had also undergone extensive chest surgery immediately prior to the development of acute psychosis, the possibility has to be considered that the stress of surgery and not INH had been the main precipitating factor. In case 2 this seems especially probable since the patient did not relapse after reinstitution of INH. It seems improbable in case 4, who improved rapidly and completely only after permanent discontinuation of INH.

In regard to improvement of the mental condition of psychotic patients during INH treatment, our experiences have been less encouraging than those published by Krieser and co-workers, who reported improvement in 44 per cent of 51 mentally ill patients and those published by Salzer and Lurie, who reported improvement of 68 per cent of anxiety and depressive states. We have seen improvement in only 17 per cent of 149 patients. Of those only one has improved very strikingly. The remainder showed only from slight to moderate improvement. Though it seems to us that mental improvement was due to INH treatment, it might have been due—at least partially—to the psychological factors provided by the environmental changes and the increased attention paid to the patients during INH medication.

We believe that our observations and those of other investigators would justify more extensive studies in this field. Those studies should include psychological testing and 17-ketosteroid output studies during and after INH in psychotic and non-psychotic patients.

SUMMARY

One hundred fifty-two patients, suffering from tuberculosis have been observed in regard to mental changes during INH medication of whom 149 had been mentally ill before INH treatment, three developed acute psychosis during INH medication. Of the 149, 17 per cent improved mentally during the treatment course and two of them (1.5 per cent) deteriorated. Three, who had been mentally normal before INH treatment, became so again after discontinuation of the drug, one only after electroshock treatment and another remained in good mental health also after reinstitution of INH. All were observed for a period from two months to two years.

SUMARIO

Han sido observados ciento cincuenta y dos pacientes de tuberculosis en relación con los cambios mentales durante la medicación con hidracida del ácido isonicotínico, de los cuales 149 tuvieron enfermedad mental previa a la administración de la medicación, tres tuvieron psicosis durante la medicación. De los 149, 17 por ciento mejoraron du rante el curso de tratamiento y dos de ellos (1.5 por ciento) empeoraron. Los tres pacientes

que habían estado mentalmente normales antesdel tratamiento con INH, volvieron a lo normal después de descontinuar la droga, uno de ellos, después de terapéutica por electro-choque y otro permaneció en buen estado de salud también después de la reinstitución del INH. Todos fueron observados pr un período desde dos meses hasta dos años.

RESUME

152 tuberculeux ont été observés en fonction des troubles mentaux dont ils furent atteints au cours du traitement par l'isoniazide. Parmi eux, 149 avaient déjà[1] présenté des troubles avant le traitement par l'isoniazide, et trois ne manifestèrent une psychose aiguë que pendant le traitement. Parmi les 149 malades, 17% eurent leur état mental amélioré pendant le cours du traitement et deux d'entre eux (1,5%) aggravé. Los trois malades qui avaient un état mental normal avant le traitement le retrouvèrent après cessation de la drogue, un seul après traitement par électrochoc, et un autre se maintint en bon état mental également après reprise de l'isoniazide. Tous furent observés pendant une période couvrant de deux mois à deux ans.

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Pulmonary Resection in Mental Patients with Tuberculosis*

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Introduction

In institutions for the mentally ill active tuberculosis occurs with dismaying frequency. Twenty-seven to 40 cases have been found per thousand examinations and the death rate due to tuberculosis in such hospitals is 19 times the death rate due to this disease in the general population.[5] The disease threatens every inmate of these crowded hospitals and there is, in addition, a more general menace for the patients form an important "seed bed" of tuberculosis which may infect those who care for the mentally ill, and indirectly, many others.

The seriousness of this problem in Minnesota was recognized early in the operation of such institutions. In 1897 H. M. Bracken,[2a] executive officer, Minnesota State Board of Health, published a medical classic titled *Should the Tuberculous Insane be Isolated from Other Inmates in Our Asylums and Accommodations Provided for Them in Separate and Detached Buildings.* The seriousness of the problem and the best known solution were emphasized. By 1907 two state hospitals had small tuberculosis units which were occupied mainly by hopeless cases. It was not until 1934 that the true tuberculosis situation in institutions for the mentally ill was determined. That year H. A. Burns[3] personally examined inmates and personnel of these institutions. He found that 82 per cent of the inmates had primary tuberculosis as manifested by the tuberculin reaction. Suggestive x-ray shadow-casting lesions were found in 11.2 per cent of whom 21.3 per cent had tubercle bacilli in the sputum. Testing of employees revealed 72 per cent with primary tuberculosis of whom 5.2 per cent had demonstrable pulmonary lesions.

In 1942 Doctor Burns was appointed chief of a new tuberculosis control unit for the express purpose of solving the tuberculosis problem in state institutions. He immediately established isolation units in four of the institutions where tuberculous mentally ill patients from all of the state hospitals could be segregated. He then arranged for examinations including x-ray films of the chests of the inmates and personnel of all institutions. Inmates found to have tuberculosis were transferred to the isolation units. This was followed by adequate examination including x-ray film inspection of the chests of all patients on admission and pre-employment examinations for personnel. Thereafter patients and personnel alike received excellent

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annual examinations for tuberculosis.[4] The establishment of four isolation units was only a temporary expediency as Doctor Burns visualized a single unit large enough to house all of the tuberculous mentally ill of the state with expert professional personnel administering the best known methods of treatment under strict contagious disease technic. He conferred with Doctor Edmund W. Miller, superintendent and medical director of the Anoka State Hospital, and other officials. It was decided that this unit should be located at the Anoka State Hospital where adequate facilities could be provided and also because of its proximity to the Medical School of the University of Minnesota. An affiliation with the Medical School was visualized whereby faculty members of appropriate departments would participate in the care of the mentally ill tuberculous patients.

Provisions were made for the remodeling of a building later described by Doctor Miller.[10] The remodeling was well underway and Doctor Burn's far-reaching vision was being realized when he died in 1949. The unit was opened in 1950 and was dedicated to his memory under the name, Herbert A. Burns Memorial Hospital in November, 1952.[2] Since his death periodic examinations of patients and personnel in all state institutions for the mentally ill has continued.

The present routine provides for 14 x 17 inch chest x-ray films of all new patients admitted to the hospitals for the mentally ill of the state, all re-admissions and all new employees. Most of the institutions also do tuberculin tests on new admissions and employees. In November, 1953, the Department of Public Welfare began making 70 mm. photofluorographic surveys of all patients and employees of these hospitals twice each year. Individuals whose photofluorograms are unsatisfactory or abnormal, and patients or employees not included in the survey are checked by 14 x 17 inch chest x-ray films within a period of 30 days after the survey. The patients whose x-ray films show suggestive evidence of tuberculosis, with or without clinical findings, are recommended for transfer to the tuberculosis unit at the Anoka State Hospital, even though they do not have positive bacteriological findings. Those presenting tubercle bacilli, except for the dangerously insane and a small group in one of the institutions for the mentally defective, are immediately transferred to the tuberculosis unit. Plans are recommended for specially designed quarters at the tuberculosis unit also for these two groups of patients.

The tuberculosis unit now consists of the Burns Hospital and three supplementary cottages with a bed capacity for 475 patients.

Since 1952 when an affiliation was started with the Surgical Department of the University of Minnesota and a surgical resident was assigned to the Burns Hospital, surgery has assumed an important part in the treatment of these patients.

Indications for Surgery

Some authors have recommended that the indications for major surgery in the psychotic patient be the same as they are in the non-psychotic.[1, 7] This is a reasonable idea but indications for surgery in the non-psychotic

are, at present, so unsettled that the use of a comparison offers no specific guidance. For example, in one report advocating identical indications for the sane and the insane, pneumothorax was the most commonly used procedure and only eight patients had excisional surgery.[7] We, too, at least to begin with, had the same general idea about treating tuberculosis in the insane, but in contrast we have used pneumothorax in no patient and have treated 131 with excisional surgery.

At the Burns Hospital we have used excisional surgery almost to the exclusion of other types of surgery and far more frequently than others who have written recently about the treatment of mental patients with tuberculosis.[1, 7, 9, 15, 16, 17] In treating these patients we have tried, first of all, to obtain arrest of the disease in the conventional sense, but beyond this we have sought to bring each patient to a state of health where he could safely be removed from the tuberculosis section and returned to the general wards of the hospital. For such a program careful selection is necessary in order to avoid further spread of the disease. We have concluded that patients about to be removed from isolation should be not only consistently free of the tubercle bacillus in gastric cultures, but that they should show no remaining evidence of tuberculosis on chest x-ray films, or at most, merely minimal, residual scarring. Even an infrequent, positive sputum arising from an apparently inactive caseous nodule could be dangerous if it were produced by an irresponsible individual in a ward. The contagious nature of the disease in this population is well recognized. Since with excisional surgery these potentially dangerous caseous nodules can be removed, we have recommended this type of surgery for all mental patients in whom the roentgenologically evident disease could apparently be taken out without undue risk. This means that some patients have had excisional surgery who, if they had been mentally competent, would doubtless have been discharged without it. In our hands the indications for sursurgery have not been the same in the psychotic and in the non-psychotic patient. Instead, excisional surgery has been used more liberally among the insane.

Preoperative Preparation

Preoperative treatment has depended, in some respects, upon the attitude of the patients. Mental patients usually fail to develop an understanding of their disease and though some may accept treatment passively, others may meet parts of the treatment with resistance. Bed-rest, for example, is impractical for most patients.

Fortunately, administration of drugs usually offers no problem and all the patients have had streptomycin twice a week and para-aminosalicylic acid or isoniazid daily before surgery for a period from a few weeks to more than a year. Recently three to four months has been the minimum length of preoperative antimicrobial administration.

Routine examinations and roentgenographic studies are not difficult to carry out though general anesthesia may occasionally be necessary for bronchoscopy, bronchograms, or planigrams.

The Operation

Segmental resection is preferred whenever possible. Other authors have adequately described the technic of doing this as well as more extensive resections[6, 12, 13] and hence it will not be detailed here. Final decision as to the extent of the resection cannot be made until the lung has been inspected and palpated. The commonest one has been segmental resection of the apical and posterior segments on the right or of the apical-posterior segment on the left. Often a wedge of the superior segment has been removed in continuity though occasionally the entire superior segment of the lower lobe has been taken. If the lingula as well as the apical-posterior segment is diseased, lobectomy has usually been done.

Thoracoplasty has been avoided, if possible, with segmental resections and it has not always been necessary with lobectomies. We prefer to do thoracoplasty simultaneously if it is used. Eleven of our 25 patients who have had unilateral lobectomies have had simultaneous thoracoplasties and three others have had thoracoplasty at a second operation.

For bilateral resections in which both sides have been done at the same operation an anterior incision has been used.[14] In males the incision is placed just above the nipples while in females it is located below both breasts and the breasts are reflected upward. The sternum is divided transversely and both pleural cavities are entered through the third interspaces. Through this incision satisfactory exposure of both upper lungs may be obtained without difficulty.

Postoperative Care

Intercostal drainage tubes are stitched in place with heavy, fishline silk so that they may not be dislodged easily if the patient becomes disturbed. Suction to these tubes is set at a negative pressure of about 20 cm. of water though stronger suction may be used if the lung does not expand to the chest wall promptly. Air leaks commonly stop in a day or two though in some cases they may persist for a week without late sequalae.

Of course, intrapleural suction alone will not bring about rapid re-expansion if the respiratory tree is blocked, and among our patients this has often been troublesome. A clear airway has been more difficult to maintain than effective intrapleural suction. If transnasal, intratracheal suction does not produce satisfactory coughing, we have promptly resorted to tracheotomy. In retrospect, we recognize that our most serious errors have been failures to use tracheotomy or bronchoscopy early enough. This has occurred in spite of the fact that we have been impressed, even from the first, with the value of these procedures in the postoperative care of the insane.

Streptomycin and para-aminosalicylic acid or isoniazid are continued for at least three months postoperatively. If the opposite side is to be done at a second operation, antibiotics are given continuously between the operations. Evaluation for discharge is done approximately one year after surgery.

Discharge and Subsequent Observation

After patients have received maximum benefit from the treatment available at the tuberculosis hospital and if they are not infectious to others, they are returned to their home institution: The following criteria are used in recommending transfer.

1. Minimum of six negative gastric cultures. (Sputum or gastric cultures are done after the antimicrobial drugs have been withheld for a period of at least two months).
2. Satisfactory x-ray examinations for a period of not less than six months for all patients who have had resection surgery.
3. Satisfactory clinical condition for a minimum period of six months.
4. At least 12 months antimicrobial treatment from the time the patients is put on drugs.

Seventy mm. x-ray films are made on these patients at six month intervals as part of the regular survey, and in addition, 14 x 17 films are made twice yearly by the staff of the hospital in which the patient is resident. These 14 x 17 x-ray films are planned to fit in so that the patient will have an x-ray film of the chest every three months. A series of three successive gastric cultures is recommended at six month intervals for at least two years after the patient is discharged from the tuberculosis unit. The frequency of cultures after two years will be determined by the patient's clinical condition and x-ray findings at his routine examinations. Any patients showing unsatisfactory clinical, bacteriological, or x-ray findings are returned to the tuberculosis unit at Anoka State Hospital for further study, and treatment if necessary.

The group of patients who do not respond to tuberculosis treatment satisfactorily and have occasional positive cultures or periods of apparent clinical activity are kept at the tuberculosis unit indefinitely.

TABLE I
Pulmonary Resections for Tuberculosis in Mental Patients

Type of Resection	Number of Patients	Deaths
Segmental	88*	1
Wedge	7	1
Lobectomy	28**	7
Pneumonectomy	8	2
	131	11 (8.4 per cent)

*Ten of these patients had staged bilateral resections and four had simultaneous bilateral resections.

**Two of these patients had staged bilateral operations and one had a simultaneous bilateral resection.

Clinical Material

Summary information concerning the resections that have been done is contained in Table I. The major resection done in each case is the basis for classification; this means that a number of the segmental patients have had additional wedge resections and some of the lobectomy

patients have had additional segmental resections. In fact, three lobectomy patients have had segmental resections of the opposite lung.

More than 100 of the operations were done by surgical residents who have served at the hospital.

Mortality: The deaths include all deaths both early and late. In the largest group, the 88 patients who had segmental resections, there was only one death even though 10 of these patients had staged bilateral resections and 4 had simultaneous bilateral resections. This one death was due to cardiac arrest during surgery in a patient undergoing a unilateral resection.

The one death in the wedge resection group was due to cirrhosis of the liver which had been undetected preoperativly.

There has been a higher mortality rate among the patients who had pneumonectomies or lobectomies. Of the seven deaths in the lobectomy group, two, one caused by a cerebrovascular accident and the other by pulmonary embolism, were probably unavoidable, and a third was a late death which occurred five months after surgery due to bilateral bronchopneumonia in a patient with an old wound infection. In a fourth patient, a 65 year old woman who died three weeks after surgery, no cause for death could be found at autopsy. Finally, three patients in this group died of causes clearly related to mistakes in surgical technic or judgment. One of these died during an operation to repair a bronchopleural fistula. In one laryngeal edema with obstruction was the main cause of death, and in the third postoperative atelectasis and pneumonia caused death on the 30th postoperative day. In both of these last two patients tracheotomies had been used but efforts to clear the respiratory tree were probably neither early nor determined enough.

The two deaths in the pneumonectomy group were due to respiratory failure. In one patient there was a massive aspiration pneumonia following surgery which led to death the following day. In the other a six-rib thoracoplasty done at the time of pneumonectomy, caused paradoxical respiration postoperatively which was never satisfactorily relieved. The patient died seven days after surgery.

TABLE II

Age Distribution by Decades. Resections for Tuberculosis.

Age	Number of Patients
11-20	1
21-30	15
31-40	27
41-50	30
51-60	39
61-70	17
Over 70	2
Total	131

Age: Tuberculosis, especially in the insane, is not limited to young adults. The average age of our patients was 47 and, as may be seen in

Table II the most frequent decade was the sixth. Many of our patients had carried relatively stable, active disease for years, perhaps since they were first admitted to the State Institutions as young people. It is worthwhile to know that even after they have grown old, excisional surgery may be used. There were 19 patients over 60 years of age, and among these there were three deaths, all in the lobectomy group. The oldest patient, a survivor, was 73.

Complications: The most troublesome and frequent, serious complication has been bronchopleural fistula; it occurred in eight and caused one death. Bronchopleural fistula has been distinguished from the less troublesome, postoperative air leak which has been persistent in 10 per cent of the segmental resections. With continuous intrapleural suction even persistent air leaks stop in a week or two without further trouble but bronchopleural fistula is accompanied by empyema, usually limited to the apex of the chest, and it demands thoracoplasty or occasionally muscle flap repairs (two cases).

Other non-fatal complications have been unremarkable except, possibly, for the occurrence of troublesome ileus in two patients. This complication was doubtless a consequence of chronic constipation and colonic distention which is common among mental patients.

Follow-Up: Early postoperative evaluation has been gratifying. Most of the operations reported here have been done less than two years ago and it will therefore be some time before a critical evaluation can be made, but because of the stable nature of the hospital population, an accurate, detailed follow-up will be possible.

Of the 120 patients (92 per cent) who are alive, 76 have had resections, or second resection if two were done, more than nine months ago. Among these 76 patients, 47 are classified as inactive, and 22 are probably inactive. The patients classified as probably inactive have satisfactory x-ray films but they have not yet had postoperative gastric, culture examinations. Seven remain who still have positive gastric cultures. The positive cultures apparently arise from the contralateral lung in three, from residual bronchial disease in two, and from an area of postoperative spread in two. We expect to obtain a satisfactory result ultimately in four or five of these seven patients.

Discussion

Excisional surgery can be successful in mental patients with tuberculosis despite the fact that their care must be unconventional in some respects. Most of what we have learned in treating these patients may be applicable only to other similar patients; nevertheless, this experience should call attention to some useful or at least provocative ideas concerning the treatment of all patients with tuberculosis.

For example, the withdrawn or indifferent attitude characteristic of many mental patients may disturb the attending staff, but it apparently need not have an adverse effect on the success of surgical treatment. It seems that neither an understanding of their disease nor a will to recover

from it are necessary. This is in contrast to conventional opinion which has generally held that a proper mental attitude was of great value in patients being treated for tuberculosis.

It appears that a healthy mental attitude is not essential, nor, for that matter, is the most widely advocated ingredient in the treatment of tuberculosis—bed rest. Prolonged bed rest has not been used for most of the patients described here. At first we did not plan to do without bed rest but its omission was the only sensible course for it could not be used routinely without the unjustifiable measures of heavy sedation or restraints. Fortunately this omission has not been critical. Does this mean that antimicrobial drugs may replace bed rest in the treatment of tuberculosis? Our meager experience can not lead to an answer for the study was not, nor could it have been, a control study of the question. It can only be pointed out that bed rest hasn't been needed for the type of patient that we have treated, and that with drugs, it may not be needed for all sane patients either.

The aggressive approach that we have taken against bilateral disease among these patients has been rewarding and such an approach may be justified, as well, for mentally competent patients with tuberculosis. If significant disease has been evident bilaterally, we have resected both sides. Already 17 patients have had bilateral resections, five of whom had simultaneous bilateral resections, and the frequency of bilateral resection among them will go up as time passes. This is due to the fact that the first patients we operated upon were often selected for surgery because their disease was unilateral, and now there are few such patients left unoperated upon.

If the disease, though bilateral, is predominantly in one lung, resection of the most diseased side may be enough. For that matter, it may not be necessary in many cases to resect either side—no one knows. The potential threat carried by a few caseous nodules is unknown, though it is a problem of great importance. It has been held that after a long course of drug treatment these nodules may become permanently harmless,[11] but since this is not established yet, we have been cautious and prefer to remove the evident disease bilaterally before allowing our patients to return to the general population of the State Hospital.

Bilateral excisions done as staged operations require a long period of treatment and even with a long interval between operations the second operation may be a trying one. Respiratory function recovers slowly on the first side and this side may then have difficulty in carrying the load of the second operation. As a trial, we have used simultaneous bilateral excisions hoping to force a bilateral distribution of the postoperative respiratory load and thus avoid some of the difficulties of staged resections. In the five patients who have had simultaneous bilateral resections, the results have been gratifying. In four of them segmental resections were done on both sides while in the fifth it was necessary to do lobectomy on one side and segmental excision on the other. Further use of this operation for selected patients is planned.

SUMMARY

1. Pulmonary resections have been done in 131 mental patients with tuberculosis. Eighty-eight have undergone segmental resections, seven wedge resections, 28 lobectomies, and eight pneumonectomies.

2. The overall patient mortality rate was 8.4 per cent. Only one of the patients who had segmental resections succumbed.

3. Whenever possible bilateral disease has been treated with bilateral resections. Fourteen who have had segmental resections and three who have had lobectomies have had bilateral operations. In five both sides have been resected at the same operation.

4. The technical problems in pre- and postoperative care which are peculiar to withdrawn, somtimes hostile, mental patients increase the difficulties of doing this type of surgery but they are not serious enough to contraindicate its use.

5. With excisional surgery as part of the treatment a large proportion of the mental patients who have tuberculosis may be brought to a state of health where isolation for tuberculosis is no longer necessary.

RESUMEN

1. Se han hecho resecciones pulmonares en 131 enfermos mentales con tuberculosis. Ochenta y ocho sufrieron resecciones segmentarias, siete resecciones en cuña, 28 lobectomías, y ocho neumonectomías.

2. La mortalidad total fué de 8.4 por ciento. Sólo uno de resección segmentaria sucumbió.

3. Siempre que fué posible se trató, la afección bilateral con resección bilateral. Catorce de los que tuvieron resecciones segmentarias y tres de los que tuvieron lobectomías tuvieron operaiones bilaterales. En cinco, ambos lados se operaron en la misma intervención.

4. Los problemas técnicos en el cuidado pre y postoperatorio-que son peculiares a enfermos retraídos, a veces hostiles, por ser-mentales aumentan las dificultades para hacer este tipo de cirugía pero no son tan serios como para contraindicar su uso.

5. Con cirugía de excisión como parte del tratamiento una gran proporción de los enfermos mentales que tienen tuberculosis pueden-ser traídos a un estado de salud en el aislamiento por tuberculosis ya no es necesario.

RESUME

1. Les auteurs ont réalisé des résections pulmonaires chez 131 malades atteints d'affection mentale et de tuberclose. 88 ont subi une résection segmentaire, 7 une résection cunéiforme, 28 une lobectomie et 8 une pneumonectomie.

2. La mortalité moyenne a été dans l'ensemble de 8,4%. Il n'y eut aucun décès parmi les malades opérés de résection segmentaire.

3. Chaque fois que cela a été possible, les localisations bilatérales ont été traitées par des exérèses bilatérales. Ces interventions bilatérales furent exécutées chez 14 malades ayant subi une exérèse segmentaire et

sut 3 qui avaient été traités par lobectomie. Dans cinq cas, les dex côtés fuent opérés en une seule séance opératoire.

4. Il convient d'utiliser dans la phase pré- et post-opératoire des soins particuliers, pour éviter les réactions parfois hostiles de ces malades atteints de psychose. Ces conditions augmentent les difficultés d'utiliser cette catégorie d'interventions, mais elles ne sont pas suffisamment graves pour être une contre-indication.

5. En faisant appel au cours du traitement à la chirurgie d'exérèse, une quantité importante de malades mentaux atteints de tuberculose sont susceptibles d'être amenés à un état de santé qui ne nécessite plus leur isolement en tant que tuberculeux.

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Massive Asthmatic Atelectasis*

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Atelectasis as a complication of bronchial asthma occurs more commonly than is diagnosed or suspected. It is usually of the lobular type and patchy in distribution. This type was first described by Huber and Koesler in 1920.[1] Many authors have suggested that status asthmaticus and even death occurring during an attack of asthma are related to lobular atelectasis.[2, 3]

Massive atelectasis, on the other hand, is much less common than the lobular type. Since Clarke[4] first described massive asthmatic atelectasis in 1930, there have been six reports published[5, 6, 7, 8, 9, 10] describing a total of 15 cases. The purpose of this communication is to present two more cases and to review the clinical aspects of this uncommon complication of a common disease.

Case 1: An eight year old boy was admitted to the Hadassah Hospital on February 28, 1952 for an acute attack of asthma. His father and one sister were reported to suffer also from asthma. The patient's first attack occurred in 1948 during hospitalization for acute nephritis. X-ray films of the chest at that time were normal. There followed five major attacks at varying intervals which necessitated hospitalization. These were usually marked by paroxysmal dyspnea, severe nonproductive cough, chest pain, wheezing and fever up to 40° C. Examination usually revealed cyanosis and tachycardia. Dullness, absence of breath sounds, and rhonchi were heard over various areas of the chest during the different admissions.

During the second admission for an asthmatic attack in Nov. 1949, x-ray film of the chest showed irregular opacities scattered chiefly over the right middle lung field. Following treatment with penicillin and streptomycin in this as well as in subsequent attacks dyspnea, fever, and x-ray findings cleared completely. During an attack, in Jan. 1950 x-ray films showed a homogeneous opacity of the right lower lobe and scattered opacities of the right upper lobe (Fig. 1).

In December 1951 he was admitted for stomatitis and treated with penicillin. There was rapid improvement of the oral lesions, but five days later a severe attack occurred, and x-ray films showed extensive opacity of the right upper and middle lobes and tracheal deviation to the right (Figs. 2 and 3). While experiencing another attack in April 1952, x-ray films showed again a similar picture (Figs. 4 and 5).

In June, 1952 he experienced still another attack, x-ray film at this time revealed an extensive, homogeneous opacity of the entire left lung with marked mediastinal shift to the left, as well as appearance of a mediastinal hernia (Fig. 6).

All these bouts of atelectasis were followed by complete clearing of clinical signs, symptoms and x-ray findings within four to 10 days following institution of therapy, usually penicillin. Between acute attacks the patient was fairly well except for symptoms of chronic bronchitis. Bronchoscopy and bronchography could not be performed because attempts at laryngeal anesthesia stimulated recurrence of asthmatic attacks.

Leucocytosis on admission varied from 11,800 to 20,400 and eosinophiles from 0 to 31 per cent of the total white count. The sedimentation rate was usually elevated up to 60/98 Westergren. No sputum could be obtained. Urine and feces were normal.

The Mantoux test was negative on three occasions but twice injections of tuberculin were followed by asthmatic attacks, without abnormal x-ray findings. Histamine injection was uneventful. The Middlebrook-Dubos test was positive in 1:128 dilution but 14 cultures of the gastric contents were negative for tubercle bacilli.

This case is remarkable for the recurrent episodes of atelectasis which was reserved on five different occasions in four years. The first time there occurred the lobular type, patchy in distribution, while in the other four times there was massive atelectasis. The highly positive Middlebrook-Dubos test and the allergic response to tuberculin with precipitation of asthmatic attacks were probably non-specific reactions.

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FIGURE 1 FIGURE 2 FIGURE 3

Figure 1 (Case 1): January, 1950. Atelectasis of right lower lobe.—*Figure 2* (Case 1): December, 1951. Atelectasis of right upper lobe.—*Figure 3* (Case 1): December, 1951. Lateral roentgenogram.

Case 2: A 15 year old girl had had asthmatic attacks which were generally preceded by rhino-pharyngitis from the age of three. Tonsillectomy was performed in 1947 at the age of nine. The tuberculin test was negative and in 1952 she received BCG. The asthma improved after the initiation of a diet consisting of vegetables and milk as well as the institution of psychotherapy. However in January 1953 she developed an unusually severe attack of asthma that lasted three days marked by cough, dyspnea and low grade fever.

Physical examination showed dullness over the right upper chest and musical rhonchi. Fluoroscopy revealed a sharply defined shadow involving the anterior segment of the right upper lobe. X-ray films (Fig. 7) showed extensive opacity of the right upper lobe with mediastinal and cardiac shift to the right. Treatment included expectorants and aminophylline. After six days, following expectoration of thick mucus, there was complete clearing of the signs of atelectasis on both, physical and x-ray examination.

Discussion

Bronchial obstruction in asthmatic attacks has been variously ascribed to bronchospasm, edema of the bronchial walls and to dyscrinie, i.e. excessive secrection of mucus of a peculiar character.

Bronchospasm is the oldest of these three theories with Laennec among its first proponents. However, it is particularly difficult to explain massive atelectasis on this basis because spastic closure of the larger bronchi is prevented by their cartilaginous rings. Most authors, on the basis of autopsy findings[2, 3] or bronchoscopy[9], have concluded that the two factors of edema of the bronchial mucosa and increased mucus secretion are the main causes of bronchial obstruction occuring in asthma. On histological examination there is found an increase in mucus—producing goblet cells, with decrease in the number of normal columnar ciliated cells. Thus, secretion of mucus is increased and at the same time there is a decrease in ciliary action thereby promoting stasis of the secretions. Dehydration resulting from the loss of fluid during increased respiratory activity tends to promote drying of the mucus into inspissated tenacious plugs that obstruct the bronchi. Such plugs are sometimes seen on bronchoscopy, and their removal is followed by prompt, clinical improvement. This process of hypersecretion of mucus and its subsequent inspissation may be so marked as to lead to laminar impaction of the mucus in second order bronchi. The bronchi become dilated and the resulting picture may simulate neoplasm, abscess formation, or tuberculosis.[12]

Massive asthmatic atelectasis occurs more commonly in childhood than in adult life because the smaller calibre of the bronchi in the child predisposes to bronchial obstruction. Of the 15 cases previously reported in the literature, five were in adults and 10 in children. This type of atelectasis is almost always unilateral and in only one of the reported cases[4] was it bilateral. Both sides are involved with equal frequency. In two cases atelectasis was segmental, in 10 the distribution was lobar, while in five an entire lung was involved. In five there was a second attack of atelectasis, while in one of the cases reported here there was a total of four attacks of massive atelectasis as well as one of the lobular type. In the other 12 cases there was only a single attack.

Massive asthmatic atelectasis is almost always accompanied by obstructive infection and fever, leucocytosis and an elevated sedimentation rate are usually found, streptococci and pneumococci occur in the sputum and

FIGURE 4

FIGURE 5

FIGURE 6

Figure 4 (Case 1): April, 1952. Atelectasis of right upper lobe.—*Figure 5* (Case 1): April, 1952. Lateral roentgenogram.—*Figure 6* (Case 1): June, 1952. Atelectasis of the left lung.

may be cultured from the mucus plugs. These organisms are usually regarded as secondary invaders. The classical roentgenological signs of atelectasis are usually present. The most helpful of these signs are those produced by shift of the mediastinum accompanied sometimes by mediastinal herniation. Elevation of the diaphragm on the affected side and contralateral compensatory emphysema are also frequently found.

On bronchoscopy obstructing plugs of tenacious amorphous material can be seen.

As is usual in allergic individuals, patients whose asthma leads to atelectasis show considerable variations in eosinophile counts. On the other hand, the presence of eosinophiles in the sputum, possibly reflecting their concentration in the lung itself, is a much more constant finding.

The fact that atelectasis is almost always accompanied by infection makes it necessary to rule out pneumonia in the differential diagnosis of massive asthmatic atelectasis. Asthmatic type of breathing with expiratory dyspnea, history of recurrent attacks of this type, eosinophilia in the blood or sputum, and X-ray findings help in differentiating between the two conditions. Fibrinous bronchitis may also cause massive atelectasis due to hypesection of a thick mucus.[13] However in this condition a long history of previous asthmatic attacks is lacking. Furthermore, the bronchial casts appear as grayish root-like formations distinctly different from the mucus plugs or the amorphous mucus in the cases of massive atelectasis of the asthmatic type.

The transient irregular, mottled, migrating eosinophilic infiltrations may tend to resemble the findings in the lobular type of atelectasis, but these conditions however do not produce such severe clinical symptoms as does asthmatic atelectasis.

Massive asthmatic atelectasis usually clears on treatment. Improvement occurs within three to five days, and within one to six weeks there

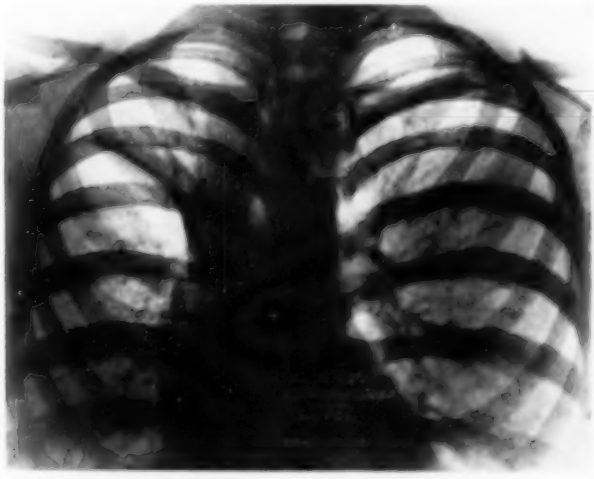

FIGURE 7 (Case 2): Atelectasis of the anterior segment of right upper lobe.

is usually complete reexpansion of the lung. The only fatal case reported was one with massive atelectasis of both lower lobes.[4] In lobular asthmatic atelectasis, on the other hand, there are many more fatal cases reported.[2, 3]

Treatment is directed at removal of the mucus plugs obstructing the bronchi, combating infection and relieving the attack.

Postural drainage, expectorants, trypsin and aerosol inhalation are helpful in relieving obstruction. Penicillin or aureomycin is used to combat secondary infection due to pneumococci and staphylococci usually found in this condition.

In the treatment of the asthmatic seizure per se, ACTH or cortisone are the drugs of choice. Aminophyline and epinephrine may be used however, and are particularly helpful in tiding the patient over until hormonal treatment takes effect. It may be possible to prevent further attacks which predispose to atelectasis by identification and removal of allergens.

SUMMARY

Massive atelectasis is a rare complication of bronchial asthma. It is caused by obstruction of the bronchi by the secretion of large amounts of thick tenacious mucus by an altered bronchial mucosa. The clinical aspects of this condition are discussed and two cases are presented.

RESUMEN

La atelectasia masiva es una rara complicación del asmabronquial. Es causada por obstrucción de los bronquios por grandes volúmenes de secreción mucosa espesa adherente producida por una mucosa bronquial alterada. Los aspectos clínicos de esta condición se discuten y se presentan dos casos.

RESUME

L'atélectasie massive est une complication rare de l'asthme. Elle est due à l'obstruction de la bronche, par une importante quantité de mucus épais et solide provenant de la muqueuse bronchique altérée. Les auteurs mettent en discussion les aspects cliniques de cet accident et en présentent deux examples.

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Editorial

THE "FUNCTIONAL" MURMUR: THE LAYING TO REST OF A GHOST

The term "functional" murmur was created about a century ago in order to separate murmurs not caused by obvious valvular deformity from the others. The most common instances were systolic murmurs of the apex or base of the heart encountered in severe anemia, pregnancy, or congestive failure, which subsequently disappeared.

In the last 30 years, some of the mechanisms causing "functional" murmurs have been clarified and can be summarized as follows:

(1) Severe tachycardia may cause a moderately loud systolic murmur. Mechanism: probably multiple (acceleration of flow, incomplete valvular closure, etc.).

(2) Severe anemia usually causes a loud apical and midprecordial systolic murmur. Mechanism: probably multiple including dilatation of the tricuspid and mitral rings (relative tricuspid and mitral insufficiency). It may also cause a loud apical and midprecordial diastolic murmur. Mechanism: dilatation of the ventricles greater than that of the a-v ostia (relative tricuspid and mitral stenosis).

(3) Conditions associated with increased blood volume (pregnancy), greater rapidity or quantity of systemic or sectional blood flow (hyperthyroidism, septal defects), or dilatation of one of the large arteries (aortitis, congenital dilatation of the pulmonary artery) frequently present a systolic murmur at the base. Mechanism: disproportion between normal ostium and dilated vessel; trigonoidation of the valve (relative aortic or pulmonic stenosis).

Further detailed explanations have been given and can be found in the various textbooks of cardiology.

Unfortunately, physicians gradually used to extend the meaning and applied the term "functional" to the following murmurs:

(a) Any murmur of persons with no history of rheumatic fever, no obvious clinical cardiac enlargement, and able to develop a normal physical activity without exertional dyspnea.

(b) Any murmur persisting for many years and unaccompanied by obvious cardiac changes or physical deterioration.

(c) Any murmur of children or adolescents which is less loud than grade 4.

The reasons for the extremely wide application of the term are obvious and frequently based on emotional factors. Upon questioning a physician on the motives which guide him in the selection of the term, the following answers are customary:

(a) "I cannot find an explanation. The child had no rheumatic fever (no proof given). He is very active (and why not?)."

(b) "The patient does not seem to have heart disease (no accurate study was undertaken)."

(c) "The child may have a little valvular damage but I would hate to tell his mother." Or: "I don't want to make a cripple of this little fellow: if I should admit a rheumatic carditis, why, that would mean putting the child to bed!"

(d) "The adolescent is pale; it must be a hemic murmur (no blood tests undertaken; if done, they reveal normal blood or a minimal anemia, quite common in persons of the same age having no murmurs)".

It is apparent that the term "functional" murmur tends to change its meaning through abuse and misuse. Created in order to depict a murmur caused by mechanisms other than permanent valvular deformity, it now tends more and more to become synonymous with "innocent" murmur. This would not be serious if better proofs of such "innocence" were available. Unfortunately, they frequently are not sought or are nonexistent. Moreover, psychological and social elements have become so utterly mixed with the term, as proved by the above statements, that actually the term has lost its original meaning and would best be abolished.

As a confirmation, the following list shows how frequently *a murmur which is definitely functional is certainly not innocent*:

— Murmurs caused by rheumatic carditis.

— Murmurs caused by severe, chronic anemia, or by vitamin deficiency.

— Murmurs caused by heart failure.

— Murmurs caused by severe dilatation of either the right ventricle (chronic cor pulmonale) or the left (coronary heart disease, hypertensive heart disease).

— Murmurs *indirectly* caused by a congenital malformation through dilatation of either or both ventricles, or dilatation of the pulmonary artery.

A few statements concerning murmurs may be useful.

(1) *A murmur not caused by valvular deformity* may be more meaningful and have a more serious prognostic value than one due to slight shrinking or irregularity of a valvular leaflet. The most common examples of such murmurs are those caused by *rheumatic myocarditis*, a process which may be silent, extremely slow, and insidious. Such murmurs may be due to relaxation of the muscular rings which surround the a-v ostia, or to edema and rigidity of the papillary muscles (systolic, apical or midprecordial murmur—relative insufficiency), or to marked dilatation of one or both ventricles (diastolic, apical or midprecordial murmur—relative stenosis). Moreover, such patients frequently have a systolic pulmonic murmur which may disappear in the subsequent course of the disease (slight dilatation of the pulmonary artery due to arteritis or increased pressure).

(2) *A murmur due to slight valvular deformity* may be the result of either unknown rheumatic fever (a common occurrence) or healed mild bacterial endocarditis. Disappearance of the murmur after a few years does not exclude a slight valvular deformity, as proved by subsequent

autopsy. While this murmur is "innocent" in the sense that no restriction of physical activity is necessary, one should consider the possibility of a recurrence of rheumatic fever and that of bacterial endocarditis. Prophylaxis is part of the treatment of these conditions. Lack of knowledge or laxity of practice would be revealed if it were not done.

(3) *A systolic murmur may be the result of a mild congenital lesion* (atrial septal defect, pulmonic stenosis). Cardiac catheterization has proved the existence of cases having no clinical symptom, no axis deviation, a systolic pulmonic murmur, and a slight increase in the gradient of pressure between right ventricle and pulmonary artery. Some of the cases are so mild that the gradient rises only during exercise (exertional increase of blood flow).

(4) *The fact that a murmur increases after exertion or when the patient lies supine,* does not exclude its being due to a valvular lesion. Exertion and recumbency increase the blood flow to the right heart and accentuate the murmurs of many congenital or acquired cardiac lesions.

Children and adolescents seen in general practice frequently present a murmur. The correct process of thinking should include:

First, an attempt to ascertain the nature of the murmur (painstakingly accurate history, good physical examination, electrocardiogram, accurate fluoroscopy with detailed study of pulmonary vessels) and, if necessary, the opinion of a cardiologist.

Second, if no evidence of the nature of the murmur is obtained, this should be carefully described in the protocol and mention should be made to the family. It should be called a "murmur of unknown cause." It would require periodic (at least yearly) check ups.

Third, in the case of apprehensive relatives, no mention of the murmur should be made but *the physician should not hide from himself* the fact that "he does not know what it is." Therefore, he should carefully describe in his notes the physical evidence and should try to obtain the periodic check ups even without mentioning the word "murmur."

Fourth, in any case where rheumatic or congenital heart disease is proved or even likely, appropriate prophylactic and therapeutic means should be undertaken.

The medical profession should be aware that frequently a murmur cannot be properly evaluated for many years. Hiding our ignorance, even if temporary, behind the cloak of a word can only hinder further progress.

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Present Status of Chemotherapy in Tuberculosis

Report of the Committee on Chemotherapy and Antibiotics

As in previous years, this report is not intended as a detailed treatise on the chemotherapy of tuberculosis, but rather as a progress report or statement on currently accepted principles and practice to serve as a guide to the physician treating tuberculosis.

General Considerations: At this writing there is no generally accepted "optimum" regimen in the chemotherapy of pulmonary tuberculosis. Streptomycin, PAS-sodium, and isoniazid are the three most commonly used drugs but there is no unanimity of opinion as to which combination is most effective. However, it is emphasized that the best results are obtained when two or more drugs are combined and given continuously for a prolonged period of time. Most investigators are agreed that chemotherapy should be given for at least a year, even in minimal cases, and in advanced cases for a total of 18 to 24 months or longer. Others feel that the drug therapy should be continued until one year *after* the patient has achieved an inactive status. It is desirable to do periodic sensitivity studies as long as the cultures remain positive.

Pulmonary Tuberculosis: The following drugs are useful in pulmonary tuberculosis:

Streptomycin and *dihydrostreptomycin* continue to be among the most effective antituberculosis agents at our disposal. Each has the same therapeutic value and the dosage is the same for both. They are generally administered in a dosage of 1 gm. twice weekly by intramuscular injection. In this dosage, streptomycin rarely causes vestibular damage, and dihydrostreptomycin rarely results in deafness. To avoid even these rather remote possibilities many physicians prefer a combination of streptomycin, 0.5 gm. and dihydrostreptomycin 0.5 gm. Hypersensitivity to streptomycin occurs occasionally, and is manifested by drug fever, rash and sometimes exfoliative dermatitis. When this occurs, the patient can often be desensitized to the drug by administering a small amount, e. g., 0.1 gm. and gradually increasing the dosage up to 1 gm. If desensitization cannot be accomplished, dihydrostreptomycin may be substituted for streptomycin. If the patient is acutely ill on admission, some workers advise that streptomycin be given daily, 1.0 gm. for thirty days, then decrease the frequency to twice weekly. Others maintain that daily administration, even at first, does not change the long term results appreciably.

Isoniazid is an extremely potent antituberculosis agent. The most commonly accepted dosage at this time is 4 to 5 mg. per kgm. of body weight daily in three divided doses. This is felt to be a safe and effective dose. Though some investigators advocate higher doses, there is little evidence to date that the larger doses are more effective. Of toxic effects resulting from the use of isoniazid, peripheral neuritis is the one most

often observed. Some investigators recommend that vitamin B_6 (pyridoxine) be given as prophylaxis to patients receiving large doses of isoniazid to prevent occurrence of peripheral neuritis. Others have found it helpful as therapy after the neuritis has developed. When used as therapy, doses of 50 to 100 mg. t.i.d. are advised. Isoniazid may cause convulsions in patients who have previously had convulsive disorders and should be used very cautiously in such patients with barbiturates added to the regimen. Psychotic episodes may likewise occur. Like streptomycin, isoniazid when used alone results in the emergence of drug resistant organisms usually after two to four months, and for this reason should be used in combination with either streptomycin and/or PAS to prolong its effectiveness.

Para-aminosalicylic acid (*PAS*) in the form of PAS-sodium remains an important agent in the antimicrobial therapy of tuberculosis. Though the optimum dosage has not yet been determined with any exactness, the dosage most commonly used in the United States today is 15 or 16 gm. daily, divided into three or four doses. Some physicians feel that dosages of 10 to 12 gm. daily may be adequate for the average patient and are willing to prescribe it in these dosages. Side reactions of anorexia, nausea and diarrhea are not uncommon and may be severe enough to warrant discontinuing the drug. Rather rarely a patient may develop a severe reaction to PAS. In some cases this simulates acute infectious mononucleosis; in others severe dermatitis may occur. In still other cases the reaction may simulate infectious hepatitis and should be recognized as an allergic response to the drug. In these cases the drug must be discontinued. Other forms of PAS such as PAS-calcium, and PAS-potassium and Rezipas have been used in an effort to lessen the undesirable side-effects experienced with PAS-sodium. The results have been something less than spectacular, however. In critically ill patients, a lyophilized form of PAS can be given parenterally to good advantage for short periods of time, e. g., in irrational patients with tuberculous meningitis.

Viomycin has a useful, though rather limited place in the treatment of the patient whose organisms are resistant to isoniazid and streptomycin, and for whom an "umbrella" is desirable for resectional surgery. The usual dosage is 2 gm. twice weekly for two or three weeks before surgery and eight to ten weeks or more postoperatively. When feasible, it should be combined with another drug to which the organisms are sensitive.

Pyrazinamide (*PZA*) is now undergoing some rather critical clinical investigations by the VA-Army-Navy group and others, particularly in combination with isoniazid. At this time no final answer is available as to its effectiveness or safety alone or in combination with isoniazid. However, it has been released by the Food and Drug Administration for distribution to institutions for use in hospitalized patients and is now commercially available. The dosage usually employed is 30 to 35 mg. per kgm. of body weight per day, the total daily dose not to exceed 3.0 gm. The dosage of isoniazid is 4 to 5 mg. per kgm. of body weight per day, the total daily dose not to exceed 300 mg. With due recognition of the po-

tential hepatotoxicity of PZA and with appropriate liver function tests conducted before and during treatment, most investigators are reporting preliminary favorable results. PZA should be discontinued promptly if significant disturbance in liver function is noted, and invariably if jaundice appears. At the present time, it is the Committee's opinion that PZA be used only under carefully controlled conditions and under the supervision of an experienced clinician.

Seromycin (*Cycloserine*) is a new antibiotic derived from a strain of streptomyces which shows promise as another effective antituberculosis agent. Epstein, Nair and Boyd reported recently on the favorable clinical results obtained in 37 patients severely ill with pulmonary tuberculosis which were treated for a 3 to 4 month period with seromycin. Though this preliminary report is encouraging, much remains to be learned concerning the drug, its assets, limitations and undesirable side reactions. It is still in the investigational stage and is now under extensive clinical trial by the VA-Army-Navy group and others. Further reports on its use will be awaited with keen interest by tuberculosis physicians everywhere.

Recommended Regimens: Though there is no generally accepted "optimum" chemotherapy regimen for pulmonary tuberculosis at the present time, recent reports of the Veterans Administration-Army-Navy and the United States Public Health Service studies indicate that the following regimens give approximately the same clinical results:

1. Isoniazid—300 mg. daily plus PAS—12 gm. daily
2. Isoniazid—300 mg. daily plus streptomycin—1 gm. twice weekly
3. Isoniazid—300 mg. daily plus streptomycin—1 gm. twice weekly plus PAS—12 gm. daily

The Veterans Administration and United States Public Health studies indicates that the regimen of streptomycin—1 gm. twice weekly and PAS —12 gm. daily is not quite the equal of the other three regimens.

Surgical Intervention in the management of pulmonary tuberculosis is still in a stage of transition. Whether all residual disease processes should be resected is a moot question. However, this Committee is firmly of the opinion, based on evidence accumulated to date, that all residual cavities and large caseous lesions should be resected in each case when this is surgically feasible. The question of the so-called "healed, open cavity" is an intriguing one, but until careful long term studies have established that such cavities are *really* healed and do not constitute a threat to the patients health, the Committee recommends their removal.

The optimum time for resective surgery in the management of pulmonary tuberculosis likewise remains a rather controversial issue. However, certain principles seem to have rather general acceptance. The disease should be well stabilized and it is preferable if the sputum is consistently negative. In the last analysis, each patient's case must be carefully studied by both the internist and the thoracic surgeon and the decision as to the time for surgical intervention is based on their combined judgment.

Acute Miliary Tuberculosis: Isoniazid has proved to be very effective in the treatment of miliary tuberculosis with survival rates of 90% and above being reported. One group has reported a 100% survival rate to date among twelve patients with the use of isoniazid alone. However, this Committee is of the opinion that streptomycin and PAS be given with isoniazid in such cases until further investigations establish with certainty that isoniazid alone is sufficient. A recommended dosage regimen is isoniazid daily, 6 to 8 mg. per kgm. body weight, for the first few months, after which the dose may be reduced to 5 or 6 mg.; streptomycin, 1 gm. daily for the first few months, then 2 to 3 times weekly; PAS, 12 to 15 gm. daily. The drugs should be continued for 12 to 18 months.

Tuberculous Meningitis: Reports during the past year indicate that survival rates of 80 to 90% are possible in tuberculous meningitis when isoniazid, streptomycin and PAS are administered for 18 to 24 months. Optimum dosage schedules are not yet determined but, pending results of further investigation, the Committee suggests a regimen similar to that for miliary tuberculosis. The Committee is of the opinion that intrathecal medication is not necessary, except perhaps in an occasional case, and may be undesirable in most cases. It is of the utmost importance to start treatment immediately if the history, physical examination and spinal fluid findings strongly suggest a diagnosis of tuberculous meningitis. If the patient's condition does not permit oral medication, the isoniazid and PAS should be given parenterally.

Genito-urinary tuberculosis responds very well in most cases to triple drug therapy with isoniazid, streptomycin and PAS-sodium in dosage as recommended for pulmonary tuberculosis. The drugs should be administered for at least a year in all such cases and longer in some instances. Recent reports from the VA studies indicate that long term therapy with isoniazid, streptomycin and PAS is very often definitive in such cases, and the need for surgical intervention is becoming surprisingly less frequent. In those cases which may require surgery, the indications and optimum time for it are best decided by the urologist, after a careful evaluation of the patient. Antituberculous therapy should be preceded by sulfadiazine or penicillin for one week to eliminate symptoms of nontuberculous infection.

Tuberculosis in Childhood: During the past two years, there has been an increasing tendency to treat active tuberculosis in children with antimicrobials, especially isoniazid. The complications such as miliary and meningeal tuberculosis which sometimes occur in active primary disease have sharply declined since the advent and use of isoniazid. Whether *all* cases of active primary tuberculosis should receive antimicrobial therapy has not yet been determined, but adherents to this view are increasing. Certainly, chemotherapy is indicated—for a year or more—in all those cases of active tuberculosis which tend to progress. In children with active tuberculosis, the physician should always be on the alert for the development of miliary tuberculosis and in those with miliary tuberculosis, routine spinal taps are indicated in order to pick up the earliest phases of impending meningitis.

Other forms of tuberculosis involving such organs and tissues as the larynx, mouth, lymph nodes, trachea, bronchi, gastro-intestinal tract and peritoneum are best treated by long term (at least a year) combined chemotherapy, using one of the regimens recommended for pulmonary tuberculosis.

Tuberculous pleurisy with effusion should be treated as a case of minimal pulmonary tuberculosis with long term continuous combined chemotherapy, for at least a year. This recommendation also applies to the so-called "idiopathic" pleurisy with effusion in patients with a positive Mantoux where careful study fails to reveal presence of tubercle bacilli in the pleural fluid. Experience has shown that in such cases the etiology is usually tuberculosis and they should be treated as such in order to avoid a reactivation later.

Committee on Chemotherapy and Antibiotics

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Teaching Chest Disease

Student Medical Care and its Teaching Influence

RUFUS F. PAYNE, M.D.*
Augusta, Georgia

Previous articles in this series have all emphasized the problem in teaching chest diseases, particularly tuberculosis, in American medical colleges today. These articles have stressed various techniques which have been developed for giving the student a better understanding of tuberculosis and have pointed out deficiencies existing, such as failure for the student to have access to the quantity and quality of clinical material needed to demonstrate the vagaries of chronic diseases such as tuberculosis.

It would appear that emphasis might also be placed on an approach that has a promise of having greater impact on the student than the ordinary methods of teaching. I refer specifically to the individual experience of the student toward tuberculosis as reflected by student health programs and the various protective techniques designed in the hope of preventing an effective exposure. The primary handicap in using this approach as an effective tool in teaching is brought about by the fact that there is a wide divergence of opinion concerning the pathogenesis, diagnosis and even clinical significance of tuberculous infection. This leaves the student with a bewilderment and frustration that not only prevents him from developing a philosophy but frequently discourages him from attempting to think through the subject for himself. Superimposed upon this bewilderment is a real fear, on the part of the students, that they may develop clinically active tuberculosis themselves and, as a consequence, clinical study of the patient is frequently neglected.

If, on the other hand, the student health service will adopt and follow a clear cut program of examination and supervision of the students themselves they would inspire confidence and would encourage clinical study.

The first consideration, I think, should be given to the protection of the medical student against infection. From past experience we can be almost certain that the student cannot escape infection as demonstrated by conversion of tuberculin hypersensitivity. On the other hand, there is every reason to believe that the dosage of organisms has a very considerable influence in the development of clinical disease and emphasis can be placed on preventing massive infection. Since the student's exposure is most likely to take place in the autopsy room and in the clinical examination of patients, it is suggested that a direct program be initiated in these fields. The student working in the autopsy room should certainly have pre-

*Superintendent, Eugene Talmadge Memorial Hospital, Assistant Professor of Medicine, Medical College of Georgia.
The fourth in a new series of articles prepared under the sponsorship of the Council on Undergraduate Medical Education of the American College of Chest Physicians.

warning that the patient has pulmonary disease and should be properly masked. The record of active clinical tuberculosis among pathologists certainly gives overwhelming clinical evidence that this protection is neglected in most places. This article is not the proper place to discuss the use of ultra-violet lights, methods of exhaust and other mechanical factors which may play an important role in the development of infection.

Routine photo-roentgen studies of the chest of every patient seen either in the out-patient department or on the wards of the hospital not only emphasizes the accepted clinical judgment that x-ray is essential in the diagnosis of tuberculosis but it also gives to the student a philosophy, or attitude, toward the clinical study of his private patients that will save him many remorseful (we hope) moments later in life. In addition to developing a sound philosophy toward the diagnosis of chest disease, it also acts as proof to the student that such measures are necessary for his protection and makes the wearing of a mask seem more of a necessity than a ritual. In the same manner, the student will not be impressed if he is required to wear a mask with every patient that he sees regardless of whether or not they have demonstrable evidence of tuberculosis. Indeed it appears at times as if this attitude encourages not only fear but even superstition among medical students and should be condemned wholeheartedly.

It is quite obvious that the usual techniques should be employed by the hospital that would guarantee that the student is duly impressed of the necessity of hand-washing, proper sputum disposal and other protective measures in all cases of pulmonary diseases until etiology is established.

Having once established confidence in the protective measures being employed in his behalf, it becomes a matter of habit to the student that he employ these same measures for the protection of other contacts of patients regardless of whether they be hospital attendants or household associates. The assurance from experience that such measures are effective in preventing spread will have a remarkable influence on the attitude of the physician toward his patient who has pulmonary disease and who, for one reason or other, may not be able to be admitted to a hospital for more effective isolation.

Having been assured that the students are being given the best protection possible against effective exposure, it becomes the responsibility of the student health service to supervise the student insofar as his own personal health is concerned. It is in this field that the greatest divergence of opinion exists and this is probably the reason why there are so many different attitudes toward tuberculosis in American medical colleges today.

It appears that there should be universal agreement on the administration of the tuberculin test on entrance to medical college. This immediately establishes, for all practical purposes, whether or not the student has had a previous effective exposure. There can be wide differences of opinion of the dose of tuberculin, but present literature indicates that 10 International Units of PPD Tuberculin is the optimum dosage. If the student is a negative reactor there are two courses of action open. The first would be to

vaccinate with BCG and follow with routine x-ray films. Regardless of what attitude the Department of Medicine would adopt toward BCG vaccination, there should be agreement on the student health program and, in my own opinion, BCG vaccination should be optional. To insist on routine re-x-ray examination of the tuberculin-negative student is poor clinical medicine and is even worse teaching. Students should understand that there is no need for routine chest x-ray films, insofar as tuberculosis is concerned, until tuberculin hypersensitivity has appeared.

If the student has a positive tuberculin test at the time of first examination, he should have routine follow-up films at not less than six month intervals. It can certainly be explained to him that x-ray examination will not prevent the development of tuberculosis nor can clinical tuberculosis always be expected to be caught in minimal stages with six-month films, but it certainly seems to be a reasonable approach and will, in most instances, disclose a lesion before it has become very extensive.

The student who was originally negative and who develops hypersensitivity while in school probably should have chest films at three-month intervals for at least two years. He should have them at less frequent intervals for the next several years, regardless of his type of practice and amount of exposure. Certainly any person who is under constant exposure to heavy doses of virulent tuberculosis bacilli should have x-ray films at least at six month intervals.

But, regardless of which measures the local medical philosophy adopts for student medical care, it is most important to appreciate the profound teaching impact of those measures. A student in the early years of his profession, like a child in the early years of his life, is more deeply subject to influence by his actual environment than by the fantasy world of lectures. It is a vital consideration in the teaching of chest diseases.

The President's Page

The physician's task is to protect and restore the health of his fellow man. Medical science has ever presented a changing picture characterized by an infinity of unsolved problems.

The incidence of disease and injury among our progenitors was greatly influenced for the better when man discovered the use of fire and learned to grow plants for food and to prepare clothing and simple shelter for his protection. Natural phenomena of violence have frequently led to a disruption of the orderly advancement of world activities but even such cataclysms as floods and famine have spurred medical men on to search for and to recognize ways and means of combating the diseases that invariably accompany such disasters.

The studies of men of the time of Pasteur and Lord Lister introduced a new era of prevention and treatment of diseases. The introduction of the microscope and the identification of bacteria opened the door for the explanation of a multitude of problems. The attention of men of medicine has been directed toward these problems with great advances being made. Yersin, Fleming and Waksman exemplify the productive type of student. Men of surgery, through the application of increasing knowledge, developed aseptic surgery which came as a boon to mankind. Increasing knowledge in the field of anatomy, pathology and biochemistry resulted in the identification of many unrecognized diseases and the introduction of effective measures for their control. The fields of epidemiology and sanitation are replete with dramatic examples of the changing tide in medicine. The control of malaria, plague, yellow fever, parasitic diseases and small pox has made it possible for man to inhabit many areas of the world that were formerly uninhabitable. Definite success in the control and cure of leprosy adds to the romance and solid satisfaction that comes from earnest endeavor in medical science.

Only a short time ago pulmonary tuberculosis was among the great killers. Increasing know-how with more effective medications are bringing tuberculosis under control. Cancer of the lung is on the increase; however, it is being hunted down and when detected early, cures are being obtained. Search for the cause of cancer is engaging the time and attention of numerous men. Cardiovascular diseases are today the leading causes of death. These diseases have come under the close scrutiny of medical men and surgeons and a new day, filled with hope, lies before the victims of all these killers.

The ever widening field of industry with its many new materials and the changing environment under which men work and man's increasing life span presage an increasing load of new medical problems.

Magnificent advances have been made in the past. To meet the challenge of the future, physicians must continue to study, investigate and experiment. In their search for knowledge they must profit from the experiences of their progenitors. They should take advantage of every opportunity to exchange information with each other through the medium of local, national and international meetings.

William A. Hudson

College News Notes

Dr. L. D. Eerland, Regent of the College for The Netherlands, Professor of Surgery and Chief of the Department at the University of Groningen, visited the United States during January and February of this year. He was accompanied by Dr. M. W. Van Weel of Rotterdam. They spent January 12-18 in Philadelphia where they visited the Bailey Thoracic Clinic, Dr. John H. Gibbon, Professor of Surgery and Director of Research Surgery at the Jefferson Medical College, as well as the other medical schools. Dr. Charles P. Bailey and Dr. Peter A. Theodos, Fellows of the College, and a group of the chest specialists in Philadelphia, arranged an informal dinner meeting for Dr. Eerland and Dr. Van Weel at the Philadelphia Country Club on Friday, January 11. Dr. Theodos is the President of the Laennec Society of Philadelphia. Drs. Eerland and Van Weel visited Minneapolis and St. Paul, Minnesota, January 17 through 22. Their program in the Twin Cities was arranged by Dr. John F. Briggs, Regent of the College for the District. They spent several days at the Variety Club Heart Hospital of the University of Minnesota with Dr. R. L. Varco and Dr. C. Walton Lillehei in the Department of Surgery. On the evening of January 21, they were the guests of the Tuberculosis Committee of the Minnesota State Medical Association at a dinner given in the Hotel Lowry, St. Paul. Drs. Eerland and Van Weel then traveled to Rochester, Minnesota to visit the Mayo Clinic. Drs. H. J. Moersch and Arthur M. Olsen, Vice President and Governor of the College respectively, received them at the clinic and a dinner was given in their honor at the Mayo Foundation House on January 24.

January 29, Drs. Eerland and Van Weel arrived in Chicago and spent the following three days visiting the hospitals and medical schools there. On Friday evening, January 28, a joint meeting of the Illinois Chapter of the College and the Chicago Tuberculosis Society was held where Dr. Eerland presented a lecture on "Surgical Resection in Pulmonary Tuberculosis; Review of 1000 Cases." Dr. Clifton Hall, Springfield, President of the Illinois Chapter, presided at the dinner meeting. Also seated at the head table with Drs. Eerland and Van Weel were Dr. James H. Stygall, Indianapolis, Indiana, President-Elect of the College, Dr. David B. Radner, Chicago, President of the Chicago Tuberculosis Society, and other officers of the College and Illinois Chapter. A photograph of the group will be found on the following page. Drs. Eerland and Van Weel left Chicago for Denver on January 30 and spent several days visiting the University of Colorado Medical Center and other institutions in that city. Dr. Henry Swann, Professor and Head of the Department of Surgery at the University, invited Dr. Eerland to observe his work during his stay in Denver, and gave a dinner in his honor at the country club. Dr. Arnold Minnig, Governor of the College for Colorado, arranged for Dr. Eerland to present a lecture at a special meeting in the medical school on February 2. From Denver, Drs. Eerland and Van Weel flew directly to New York City to meet their steamship sailing date for return to Europe. Unfortunately, it was necessary to cancel their proposed visit to Boston before departure, due to the scarcity of time. A planned trip to Washington, D. C. also had to be cancelled.

STATE SOCIETY HONORS COLLEGE PRESIDENT

Dr. William A. Hudson, Detroit, President of the American College of Chest Physicians, was honored by the Michigan State Medical Society at a dinner held at the Sheraton-Cadillac Hotel, Detroit, on March 10.

The Michigan State Medical Society sponsored the dinner for the presidents of national medical associations who are members of the state society.

The patients of Dr. Hudson presented him with a bound volume of letters of congratulation upon his many achievements during the past thirty years and a color television set in appreciation of services rendered to them over the years.

ERRATUM

On page 473 of the April issue of DISEASES OF THE CHEST, the name of the President of the Michigan Chapter of the College was given erroneously. Dr. William H. Barron, Detroit, is the President of the chapter.

JOINT MEETING, ILLINOIS CHAPTER, AMERICAN COLLEGE OF CHEST PHYSICIANS AND CHICAGO TUBERCULOSIS SOCIETY

Some of the physicians who attended the Joint Meeting held in Chicago, January 28, in honor of Professor L. D. Eerland, Groningen, The Netherlands.

Obituary

JOHN ALEXANDER

Educator, Crusader and World-Renowned Chest Surgeon

1891-1954

Few persons have died leaving such contributions to humanity and such a rich heritage to present and future generations as did John Alexander. His life was all the more significant because he labored and accomplished under handicaps that would be unbearable to many of us.

He was born in Philadelphia on February 24, 1891. At the age of 10 years, he attended Episcopal Academy, Philadelphia, for one year. From 1902 to 1908 he was a student in Chestnut Hill Academy, Pennsylvania. At the age of 21 years, he received the degree of Bachelor of Science, University of Pennsylvania, one year later the degree of Master of Arts in English Literature, and in 1916 the degree of Doctor of Medicine.

While a student he won numerous prizes, consisting of one in botany in 1910, the French prize for an essay written in 1911, the Undergraduate Medical Association Prize in Anatomy in 1913, the Doctor Spencer Morris Prize for passing the best examination for the degree of Doctor of Medicine in 1916, the Frederick A. Packard Prize for the greatest proficiency in the course in Internal Medicine in 1916, and the Professor of Obstetrics Prize in 1916. He found time for extracurricular activities. He was captain of the varsity crew, president of the Arts Association, advisory editor of the Pennsylvanian, president of his first-year medical class and president of the Undergraduate Medical Association.

He served with the French Army in 1916 and with the American Army in the United States and France in 1917-18. In 1919 he received a certificate in surgery and anatomy from the University of Lyon, France, and upon his return to this country he served as assistant instructor to the professor of clinical surgery at the University of Pennsylvania during part of 1919 and 1920.

In 1920, Dr. Alexander was appointed to an instructorship in surgery at the University of Michigan. He advanced to assistant professor in 1925, associate professor in 1930, and full professor in 1932, which rank he held until his death. Thus he devoted his entire teaching career of 34 years to one institution and contributed significantly to the fine reputation of the department of surgery of that school. Through the years he acquired and transmitted to his students the best and most modern information in his field. From 1928 to 1931, inclusive, he did postgraduate work at Paris, Lyon, Berlin, Hamburg, and London. In 1929, at the University of Michigan, he received the Henry Russell Award for distinguished scholarship or authorship and conspicuous ability as a teacher.

Dr. Alexander was a most popular teacher both among undergraduate and graduate students. He trained 79 chest surgeons. Dr. F. A. Coller, head of

his department, said, "He was a truly great teacher, and hundreds of his disciples now project his example and his learning over the whole world." One of the finest compliments came from Dr. F. A. Coller, who said, "He was a crusader as well as a great surgeon in the fight against tuberculosis." His capacity as a crusader was known everywhere and one wonders if this did not save and extend as many or more lives as his other activities. In addition to local teaching, Dr. Alexander taught physicians of the world by describing and reporting his work and accomplishments. Ninety-five articles from his pen on thoracic diseases and surgery appeared in American and foreign medical journals.

In 1925, his first book appeared under the title, *Surgery of Pulmonary Tuberculosis*. This was the first of its kind in the English language and was introduced by Hugh Cabot and Edward R. Baldwin. In 1937, a much larger book appeared under the title, *The Collapse Therapy of Pulmonary Tuberculosis*. This book was based on experience with surgical treatment of approximately 1800 patients, a study of 1700 articles and books, and observations made during visits to many leading thoracic surgery clinics in this country and abroad.

Dr. Alexander was frequently called upon for special lectures before numerous medical organizations and learned societies in this country and abroad, including the Abner Wellborn Calhoun Lecture Medical Association of Georgia, 1941, the Trudeau Memorial Lecture, Saranac Lake, 1942, the Henry Russell Lecture, University of Michigan, 1944, and the Mary Scott Newbold Lecture, Philadelphia, 1945.

In addition to his duties as professor of surgery, Dr. Alexander was surgeon in charge of the section of thoracic surgery, department of surgery, University of Michigan Hospital. He was greatly in demand as a consultant, having served in this capacity as civilian consultant in thoracic surgery to the United States Army to 1946 and counselor in thoracic surgery, Special Medical Advisory Group of the Administrator of Veterans' Affairs to 1946. He was chief surgeon of the Michigan State Sanatorium and consultant in thoracic surgery at three other sanatoriums in that state. He was honorary consultant to the Surgeon General, United States Navy, from 1951 to July 16, 1954, and consultant in thoracic surgery at the Veterans' Administration Hospital in Ann Arbor.

Patients came to Dr. Alexander from almost everywhere as he was held in such high regard both abroad and at home. Perhaps Dr. Alexander's most famous patient was Senator Arthur H. Vandenberg of Michigan. Dr. Alexander's influence on patients and their thorough appreciation of his work and goodness is expressed in the following quotation in a letter from a patient at the Michigan State Sanatorium: "Dr. Alexander had trodden the long, hard road from the domination of the tubercle bacillus and could give to his patients not only the physical aid of his marvelous skill and knowledge, but his sympathy and understanding. Thus he helped us over the rough places, back from the devious bypaths, across the desert with its cruel mirages, from the mistaken divergences, reaching forth his hand to us when we stumbled, and holding out to us a torch in the darkness."

His great attainment, geniality, and understanding placed him in demand in medical organizations. He honored and graced those fortunate enough to claim him as a member. He held memberships in 30 medical societies, 11 of which are in foreign countries. He was president of the American Association for Thoracic Surgery in 1935. In 1944, he was vice-president of the National Tuberculosis Association, and in 1945 president-elect of the American Trudeau Society. He was a member of the Founders' Group of the American Board of Surgery (1937), and also a member of the Founders' Group of the Board of Thoracic Surgery (1948).

Following graduation in medicine, Dr. Alexander continued to win honored prizes, including the Quinquennial Samuel D. Gross Prize in 1925 and the Trudeau Medal of the National Tuberculosis Association in 1941. In 1940, the University of Pennsylvania conferred upon him the honorary degree of Doctor of Science. In 1953, he was granted the Bruce H. Douglas Award of the

Michigan Trudeau Society and in 1954 the University of Pennsylvania Varsity Club Award of Merit.

Throughout student years, he apparently was in good health. Pleurisy with effusion developed in January 1921. He went to Saranac Lake in November and entered Trudeau Sanatorium in January 1922. He proceeded to control his own disease and at every turn he helped others throughout the remainder of his life. This applied not only to patients, but also to students and graduates in medicine and nursing, as well as the citizenry everywhere. There is probably no better example of a physician turning adversity into opportunity. This began with his first illness and continued throughout his life.

In his introduction to the book of 1925, Dr. Baldwin said, "Dr. Alexander has done us a valuable service under difficulties which those who know him will aways consider extraordinary." Dr. Baldwin was referring to the fact that Dr. Alexander prepared much of the manuscript for this book while being treated for tuberculosis of the spine. He both read and wrote while in a plaster body cast and lying on a Bradford frame with a personally-devised writing board to which he reached and looked upward. This was one of the truly dramatic incidents in medical writing. His courage, tenacity of purpose, and a burning desire "to acquaint the medical profession with the principles and practical details that will enable it each year to save thousands of lives which will be lost if surgery is not undertaken," drove him to overcome the obstacles presented by his illness and to write his first book.

Beginning in the early 1930's, Dr. Alexander spent part of each winter, except for about four years in the late 1940's, resting in Tucson, Arizona. During one recurrence of illness which took him from his usual activities, he rewrote his book, the large volume on collapse therapy (1937). Another manifestation of his fine spirit was exhibited when he was president-elect of the American Trudeau Society (1947). He declined the honor of the presidency because of illness which he thought would not permit him to do justice to the organization.

He saw the chest, including the heart, yield up its secrets to the surgeon and he himself contributed mightily to the unfolding of these secrets. He pioneered in medical education and surgical techniques of the lungs and the heart. In 1936 he married Emma Ward Woolfolk, who survives him.

After numerous bouts with tuberculosis, in each of which he was ultimate victor, John Alexander died from gastrointestinal hemorrhage on July 16, 1954. The principles he taught, the operations he perfected or devised, the courage he manifested, and the cheerfulness and encouragement he transmitted, will cause his great name to continue to resound around the world.

J. Arthur Myers

ANNOUNCEMENT

The Department of Laryngology and Bronchoesophagology, Temple University Hospital and School of Medicine, will present the following postgraduate courses, arranged under the direction of Drs. Chevalier L. Jackson and Charles M. Norris:

Postgraduate Course in Bronchoesophagology
June 13-24, 1955
October 17-18, 1955

Postgraduate Course in Laryngology and Laryngeal Surgery
September 19-30, 1955

Tuition for each course is $250. Further information and application forms may be obtained from Dr. Chevalier L. Jackson, 3401 North Broad Street, Philadelphia 40, Pennsylvania.

MEDICAL SERVICE BUREAU

Position Wanted

Position wanted in field of tuberculosis, any capacity. On staff of large sanatorium since 1938: chief, medical service, '41-44; assistant superintendent since '44. Nearing retirement on reaching statutory age limit of 70. Native American, active, in good health, no dependents. Position and pay secondary. Address Dr. John M. Stanley, Assistant Superintendent, Glenn Dale Hospital, Glenn Dale, Maryland.

Positions Available

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The New York State Department of Health has an opening for a Public Health physician who has specialized in the diagnosis and treatment of tuberculosis, including the interpretation of chest x-ray films. Entrance salary is $10,470 with 5 annual increments to $12,510. State service provides one month's vacation, liberal sick leave, and participation in state retirement plan. Qualifications include citizenship, possession of, or eligibility for a New York State medical license, and 4 years of specialized tuberculosis experience. Duties may include consultative work with staff of mental hygiene hospitals or local health departments in the development of tuberculosis control programs. Further information may be obtained from Mr. Richard M. Mattox, Director, Office of Personnel Administration, New York State Department of Health, State Office Building, Albany 1, New York.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

21st Annual Meeting, American College of Chest Physicians
Ambassador Hotel, Atlantic City, New Jersey, June 2-5, 1955

Fourth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Cologne, Germay, August 19-23, 1956

POSTGRADUATE COURSE

10th Annual Postgraduate Course on Diseases of the Chest
Hotel Knickerbocker, Chicago, Illinois, October 3-7, 1955

CHAPTER MEETINGS

New York State Chapter, Buffalo, May 12
Michigan Chapter, Detroit, May 13
Illinois Chapter, Chicago, May 18
Minnesota Chapter, Minneapolis, May 23
Arkansas Chapter, Hot Springs, May 29

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1. Hyman, S., and Rosenblum, S. H.: Illinois M. J. 104:257, 1953.
2. Piper, C. E., and Nicklas, F. W.: Industr. Med. 23:510, 1954

*U.S. Pat. 2,628,181

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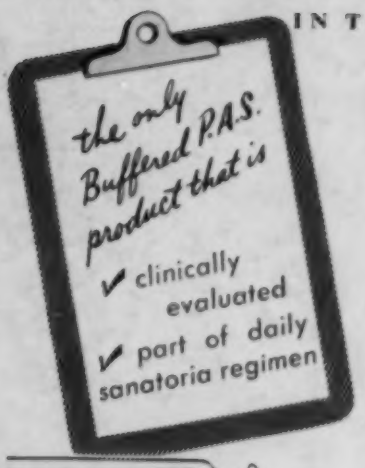

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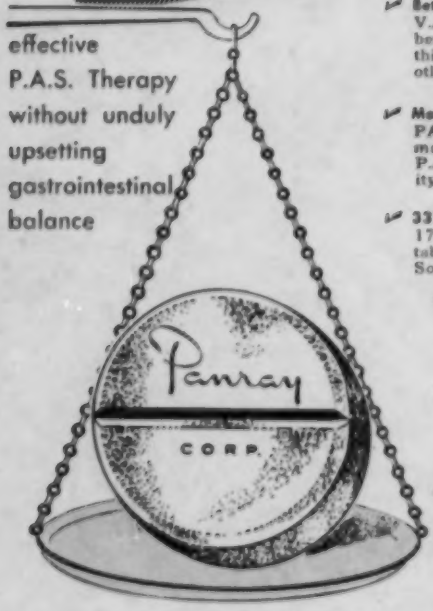

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References

(1) V.A. Quarterly Prog. Report, April '53

(2) V.A. Quarterly Prog. Report, Oct. '54

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